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HISTOLOGIC EFFECTS OF VARIOUS SCLEROSING SOLUTIONS

USED IN THE INJECTION TREATMENT OF HERNIA

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In 1880 Billroth made the statement that if any one could find a solution that would produce artificial proliferation of tissue the problem of the radical surgical treatment of hernia would be solved. In recent years Hall,[1] Wolfe,[2] Mayer,[3] Bratrud,[4] Rice,[5] Quillin,[6] Fowler,[7] La Rochelle[8] and many others have reported clinical cures with the injection of different sclerosing solutions in selected cases of hernia, without any serious complications. The only experimental studies of the effects of some of the solutions used have been made by Hall, Wolfe, Rice and Bratrud. Hall, using dogs, guinea-pigs and monkeys, injected from 1 to 5 cc. of Piña Mestre's solution into the abdominal muscles daily for from five to six days and found at the end of that time a marked

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3. Mayer, Ignatz: Treatment of Hernia by Subcutaneous Injection, M. J. & Rec. **125**:596 (May 4); 672 (May 18) 1927; Corrective Treatment of Hernia by Subcutaneous Injections, ibid. **135**:275 (March 16) 1932.

4. Bratrud, A. F.: Ambulant Treatment of Hernia, Journal-Lancet **54**:337 (June 15) 1934.

5. Rice, Carl: The Rationale of the Injection Treatment of Hernia, Minnesota Med. **18**:623 (Sept.) 1935.

6. Quillin, Lawrence J.: Injection Treatment of Reducible Hernia, Internat. J. Med. & Surg. **47**:394 (Oct.) 1934.

7. Fowler, Samuel: Experience with the Injection Treatment of Hernia, M. Rec. **141**:207 (Feb. 20) 1935.

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proliferation of fibroblasts and endothelial cells with many foreign body giant cells. Sections of tissue from the monkeys showed extensive mechanical rupture and necrosis of muscle fibers. In places there were numerous multinucleated regenerating muscle buds and single myocytes. Wolfe used rats and injected the same solution six times daily into the abdominal muscles. Microscopic examination showed a distinct proliferation of fibroblasts, but no mention was made of any other tissue changes. Bratrud, using dogs and rabbits, injected a solution composed of phenol, alcohol and Lloyd's specific tincture of thuja; in addition, he used solutions of tannic acid in strengths from 0.5 to 5 per cent and also Piña Mestre's solution. He injected 1 cc. of the solutions weekly for six weeks before examining the tissues. Microscopic study showed a marked proliferation of fibroblasts dipping down between muscle fibers. There was no infiltration of polymorphonuclear cells or any evidence of necrosis, except in the tissue of rabbits into which Piña Mestre's solution was injected, as noted by Hall. No giant cells were found. Fibrosis was more marked with the solution of tannic acid than with the solution containing thuja. Injection into the peritoneum caused no abscess formation but produced marked proliferation of fibrous tissue so as to obliterate the peritoneum completely. Rice, experimenting with dogs, first used the Bratrud solution but soon discarded it because when used in doses larger than from 4 to 5 minims (0.2 to 0.3 cm.) tissue necrosis was produced. He then used sodium psylliate (sylasol) and cut sections at intervals of fifteen hours and five, eight, fourteen, eighteen and forty-two days after injection. In sections obtained fifteen hours after injection he noted an exudative reaction of polymorphonuclear leukocytes with few fixed connective tissue cells and some necrosis of the muscle, and subsequent sections showed a gradually changing fibroblastic reaction of fibroblasts into a mature fibrous tissue in from eighteen to forty-two days.

Since so limited an amount of comparative experimental work has been done, it is difficult to evaluate the actual results of the injection treatment of hernia and the value of the different solutions so widely recommended. It seems obviously important to know what histologic changes occur and what type of repair follows at various intervals.

In this experimental study four solutions, namely, galtanol, sodium psylliate, Bratrud's solution and a modification of Mayer's solution, which have been strongly advocated and used with good clinical results, and Carabba's solution and a solution of iodine and tannic acid were used in order to compare their histologic effects.

The injection method of treating hernia was first used about a hundred years ago. Velpeau [9] in 1835 used injections of a solution of

9. Velpeau, A. A. L. M., cited by Marcy, H. O.: The Anatomy and Surgical Treatment of Hernia, New York, D. Appleton & Co., 1892, p. 272.

iodine with results he claimed to be successful. Pancoast,[10] of the Philadelphia General Hospital, improved the technic and in 1836 reported the use of equal parts of compound solution of iodine and tincture of cantharides in 13 cases. A few years later Heaton,[11] of Boston, reported the cure of hernia by the injection of a solution of Quercus alba and continued to report good results until 1877. In the same year Schwalbe,[12] of Germany, used 70 per cent alcohol. A few years later the injection of liquid petrolatum became popular, but the results were poor, and an unfavorable opinion of this method arose, which has persisted to the present time. In 1901 Lannelongue [13] reported good results with a 10 per cent solution of zinc chloride. In 1927 and 1932, Ignatz Mayer, of Detroit, reported over 3,000 cases in which he had used the injection method in the past twenty-five years, with recurrences in less than 2 per cent. During the same period, Piña Mestre,[14] of Barcelona, Spain, reported over 15,000 cases in which his solution was used, with recurrences in less than 2 per cent. In 1934 Bratrud reported successful treatment in over 400 cases, with recurrences in less than 4 per cent after two years. In 1935 Fowler reported successful treatment with galtanol in over 700 cases, with recurrences in less than 4 per cent. In the same year Rice advocated the use of sodium psylliate as being very effective histologically and not toxic or destructive to tissues.

With the improvement of the technic and more careful management of these cases and the use of well selected sclerosing solutions, the general tendency is toward a more rational consideration of this method by those who have been sufficiently interested to investigate this procedure. The aim of the treatment is to stimulate the production of large amounts of fibrous tissue firmly rooted in the adjacent defective muscle and fascia, with as little inflammatory exudation or reaction as possible. If sufficient scar tissue can be produced to constrict the internal and external inguinal rings and obliterate the canal, the end-result may be similar to those obtained with operative treatment, except for the removal of the sac. By the injection method the sac remains empty, functionless and compressed by the surrounding proliferation of fibrous tissue, so that it is not only unnecessary to obliterate it but extremely

10. Pancoast, cited by Marcy, H. O.: The Anatomy and Surgical Treatment of Hernia, New York, D. Appleton & Co., 1892, p. 272.

11. Heaton, George: Radical Cure of Hernia, Boston M. & S. J. **29**:217, 1843.

12. Schwalbe, cited by Sultan, G.: Atlas und Grundriss der Unterliebsbrüche, Munich, J. F. Lehmann, 1901.

13. Lannelongue, O. M.: Un tour du monde, Paris, Libraire Larousse, 1909, pp. 296-297.

14. Mestre, P.: Las injecciones proliferantes obturadoes en las hernias, abstr., J. A. M. A. (edición en español) **18**:816 (Dec. 15) 1927.

Explanation of Figure 1

Fig. 1.—*A*, section of tissue obtained twenty-four hours after the injection of galtanol. This section shows slight edema with a marked cellular reaction in the subcutaneous area and between the muscle bundles. The cells are chiefly polymorphonuclear leukocytes, although some lymphocytes and large mononuclear cells can be made out. A few fibroblasts are also present. The upper area shows a ruptured blood vessel. *B*, section of tissue obtained seven days after the injection of galtanol. This section shows marked proliferation of fibroblasts extending deeply between the muscle bundles. The fibroblasts are assuming a parallel formation, being separated by young fibrous tissue. The fibroblasts are large and stain deeply. Many new capillaries can be seen throughout the section. Several lymphocytes and wandering cells are scattered throughout the section, but no polymorphonuclears are present. *C*, section of tissue obtained two weeks after the injection of galtanol. This section shows a much denser area of proliferating connective tissue extending between muscle bundles. The fibroblasts are more elongated and are arranged in parallel layers separated by more deeply staining strands of fibrous connective tissue. Many multinucleated giant cells are present; there are also a few lymphocytes. *D*, section of tissue obtained eight weeks after the injection of galtanol. This section shows a more mature fibrous tissue adjacent to muscle substance in which many multinucleated giant cells are still present. These are filled with brownish granules. *E*, section of tissue obtained eight weeks after the injection of galtanol. This is another area of section *D*, which shows a dense mature fibrous tissue firmly adherent to the muscle substance and dipping in between the muscle bundles to a slight extent.

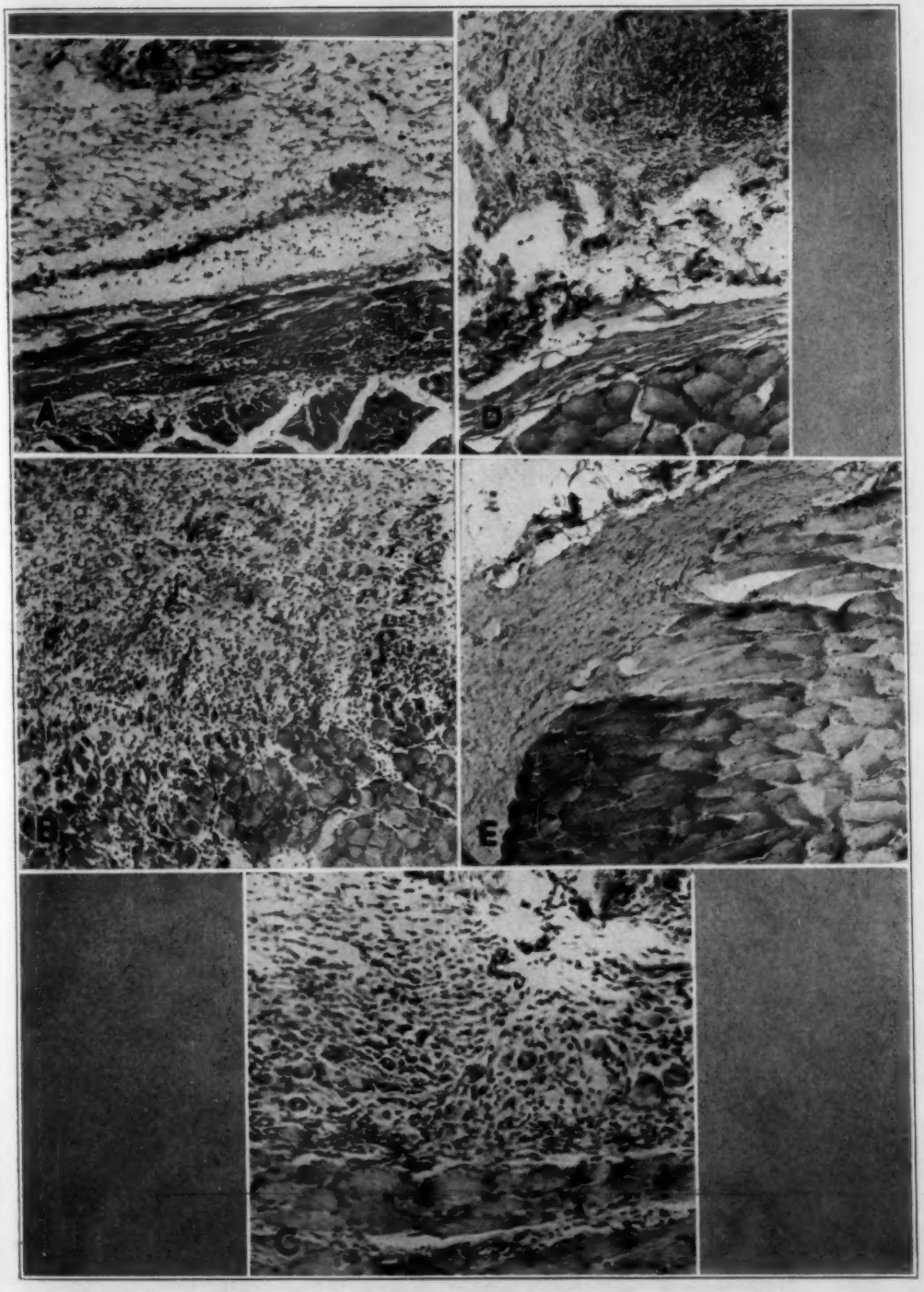

Figure 1

dangerous to inject the sclerosing solution into it because of the chemical peritonitis that would result. In a great number of cases in which operative treatment would be hazardous because of age, physical defects or repeated operative recurrences, this method would be of great value.

In order to obtain good results, the sclerosing solution should be one that (1) causes no pain, (2) is not injurious to the tissues, (3) does not produce a systemic reaction, (4) produces a minimum of inflammatory reaction with a marked proliferative phase, (5) produces marked fibrosis to fill up the defect with firm scar tissue and (6) does not produce peritoneal inflammation if inadvertently injected into the peritoneal cavity. With these points in mind and in view of the absence of any recorded comparative study, the experiment was undertaken to compare the relative merits of each solution to be tested.

EXPERIMENTAL PROCEDURE

Adult rats were used. On each side of the ventral abdominal wall a sclerosing solution was injected subcutaneously in an attempt to have the point of the needle reach the abdominal muscles. The amount of the substances varied from 3 to 8 minims (0.18 to 0.5 cm.). The following solutions were used:

Galtanol

A hydro-alcoholic tincture of selected botanic extracts of gallic and tannic acid

Sodium psylliate (sylasol)

A 5 per cent solution of a vegetable oil extracted from the seed of the psyllium groups

Bratrud's solution

Phenol	50 parts
Alcohol	25 parts
Lloyd's specific tincture of thuja	25 parts

Modification of Mayer's solution

Zinc sulfate	4.0 cc.
Phenol	24.0 cc.
Glycerin	15.0 cc.
Aqueous solution of butyn (0.1%)	100.0 cc.

Tannic Acid and Iodine Solution

Tannic acid	1.3 Gm.
Iodine	4.0 cc.
Alcohol	30.0 cc.
Double-distilled water	60.0 cc.

Carabba's solution

Phenol	45.0 cc.
Sodium borate	1.04 Gm.
Salicylic acid	1.04 Gm.
Glycerin	120.0 cc.
Spirit of camphor	240.0 cc.

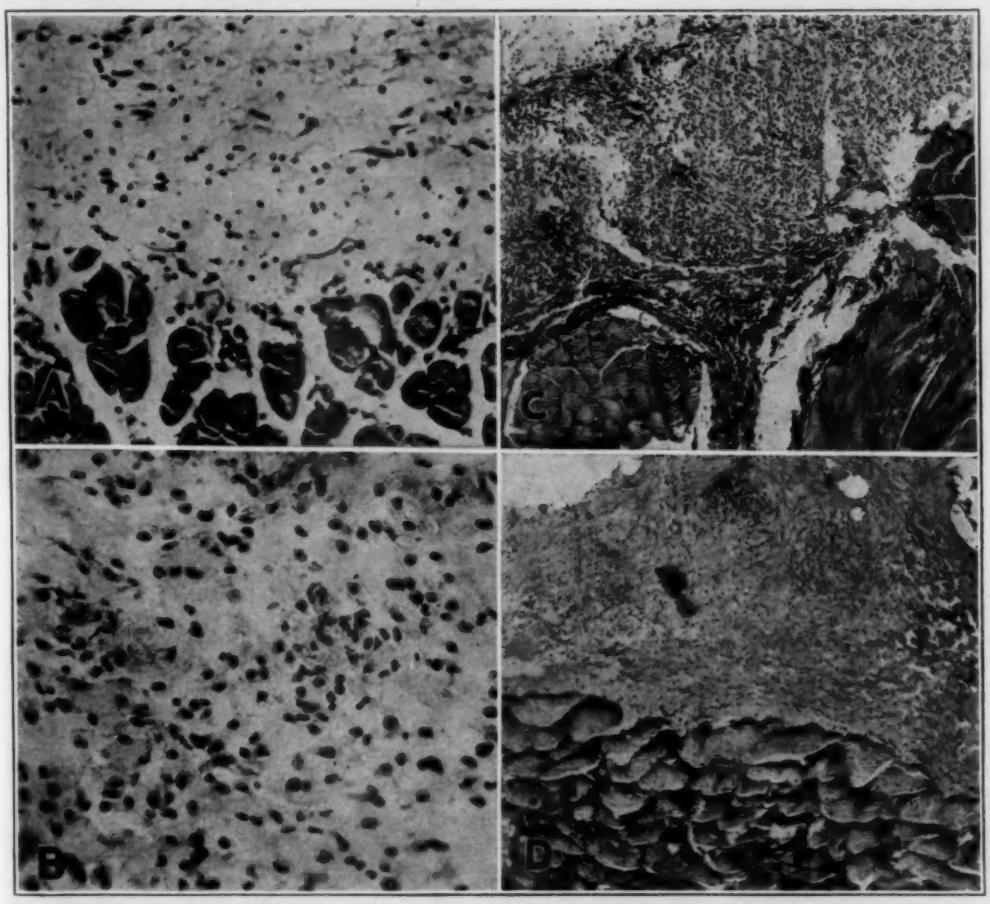

Fig. 2.—*A*, section of tissue obtained twenty-four hours after the injection of sodium psylliate. This section shows moderate edema of the subcutaneous tissue and between the muscle bundles and slight necrosis of muscle cells. There are few fibroblasts, some polymorphonuclear leukocytes, lymphocytes and large mononuclear cells. *B*, section of tissue obtained seven days after the injection of sodium psylliate. This section (high power magnification) shows a marked proliferation of fibrolasts. There are many wandering leukocytes and a few lymphocytes, but no polymorphonuclears are present. *C*, section of tissue obtained fourteen days after the injection of sodium psylliate. This section shows a great amount of fibroblastic reaction adjacent to muscle tissue and dipping down between the muscle bundles. The fibroblasts are flattened out and held together by coarse bundles of fibrous tissue. There are several wandering leukocytes. *D*, section of tissue obtained eight weeks after the injection of sodium psylliate. This section shows a dense area of adult firm fibrous tissue closely adherent to and dipping to a slight extent between the muscle bundles.

EXPLANATION OF FIGURE 3

Fig. 3.—*A*, section of tissue obtained twenty-four hours after the injection of Bratrud's solution. This section shows slight edema of the muscle bundles with a polymorphonuclear leukocytic reaction. In the inflammatory exudate there are also several histiocytes and a few fibroblasts. There is slight necrosis of muscle cells. *B*, section of tissue obtained seven days after the injection of Bratrud's solution. This section shows a marked fibroblastic reaction extending into the muscle tissue. The fibroblasts are elongated and are held together by strands of fibrous tissue. There are many newly formed blood vessels throughout, several lymphocyte and wandering leukocytes. *C*, section of tissue obtained two weeks after the injection of Bratrud's solution. This section shows fibrous tissue between the muscle bundles. It is denser than that in section *B*, and the fibroblasts are much smaller and thinned out. There are many lymphocytes, wandering leukocytes and also several multinucleated giant cells. *D*, section of tissue obtained three weeks after the injection of Bratrud's solution. There are coarse bundles of fibrous tissue adjacent to the muscle that appears more mature than those in section *C*. No giant cells or other cells are noted. *E*, section of tissue obtained eight weeks after the injections of Bratrud's solution. This section shows an adult dense fibrous tissue. The nuclei of the fibroblasts are very small and widely separated by the collagenous tissue.

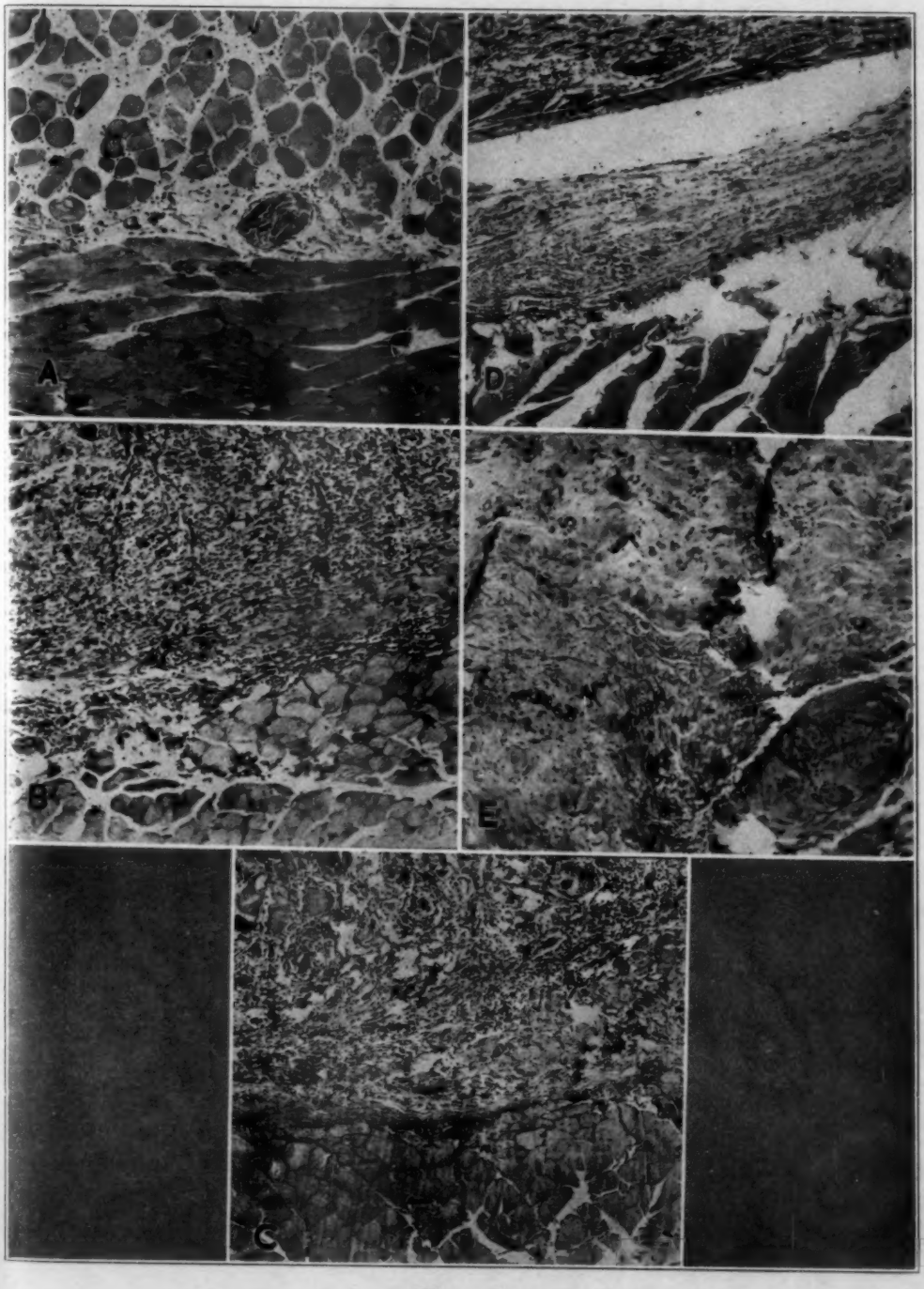

Figure 3

EXPLANATION OF FIGURE 4

Fig. 4.—*A*, section of tissue obtained twenty-four hours after the injection of iodine and tannic acid solution. This section shows a fibrinous exudate in which there are many polymorphonuclear leukocytes. In the lower part of the section is an abscess. Throughout are lymphocytes, fibroblasts and a few large mononuclear cells. *B*, section of tissue obtained three days after the injection of iodine and tannic acid solution. This section shows a proliferation of great numbers of fibroblasts in the fibrinous plastic exudate. There are many endothelial and transitional leukocytes present as well as some lymphocytes. A few polymorphonuclears are still to be seen. *C*, section of tissue obtained seven days after the injection of iodine and tannic acid solution. This section shows a more adult fibrous tissue in which the fibroblasts are smaller and fewer in number. There are several new blood vessels throughout. Few lymphocytes are present. *D*, section of tissue obtained two weeks after the injection of iodine and tannic acid solution. This section shows a more mature fibrous tissue in which the nuclei are much smaller and faintly staining. The tissue appears to be composed of coarse strands of fibrous tissue closely bound together. There are many lymphocytes and wandering leukocytes throughout the new fibrous tissue. *E*, section of tissue obtained eight weeks after the injection of iodine and tannic acid solution. This section (high power magnification) shows an adult dense fibrous tissue in which the nuclei are small and compressed into spindle shapes.

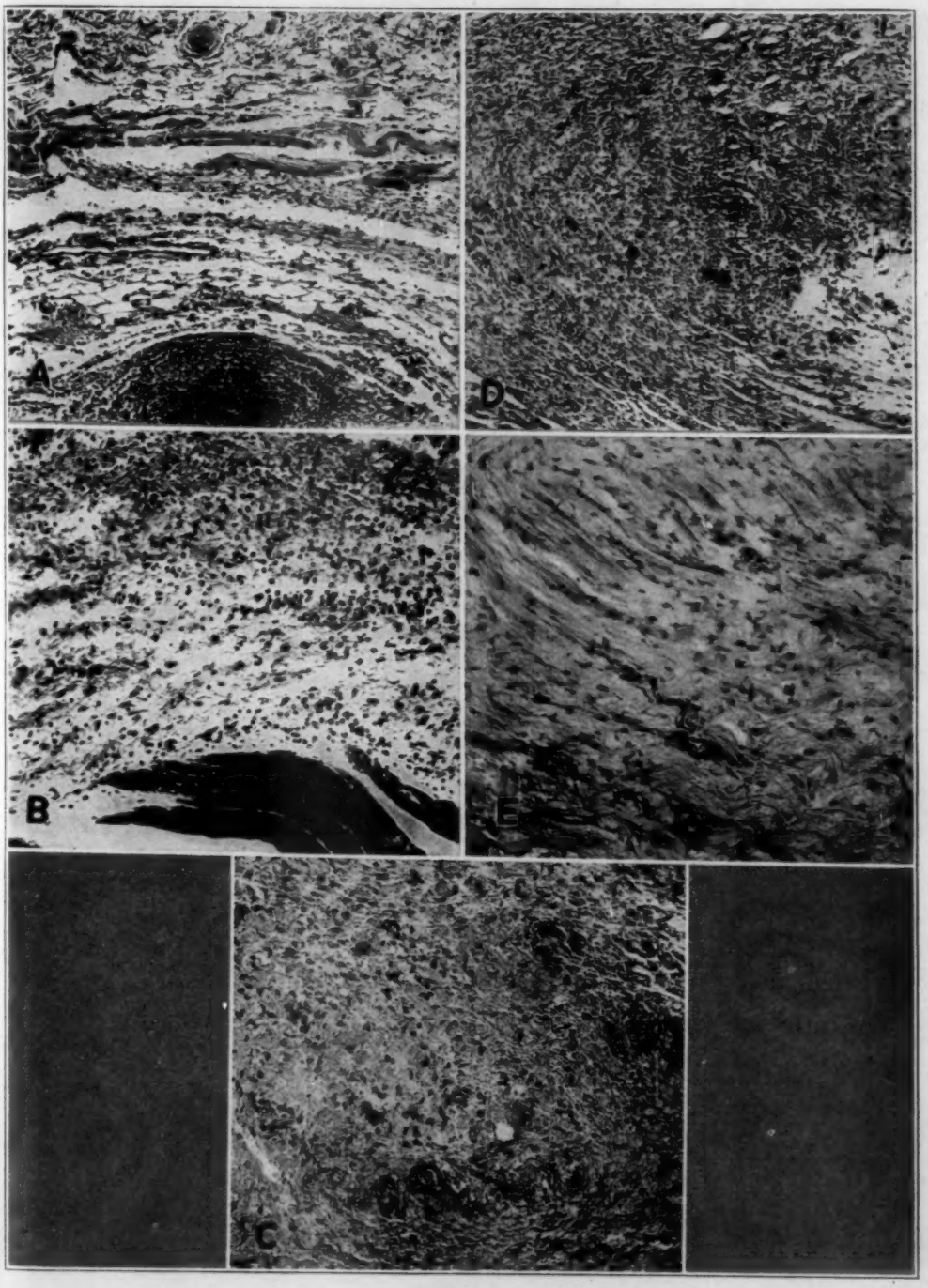

Figure 4

EXPLANATION OF FIGURE 5

Fig. 5.—*A*, section of tissue obtained twenty-four hours after the injection of Carabba's solution. This section shows a marked exudative reaction in the subcutaneous area and extending between the muscle bundles. In the fibrinous exudate there are many polymorphonuclear leukocytes, fibroblasts, several endothelial leukocytes and also a few lymphocytes. *B*, section of tissue obtained seven days after the injection of Carabba's solution. This section shows a marked proliferation of fibroblasts extending into the muscle tissue. The intercellular substance is loose and faintly staining. There are many multinucleated giant cells present throughout the section. *C*, section of tissue obtained two weeks after the injection of Carabba's solution. This section shows a more mature fibrous tissue adjacent to the muscle section. The nuclei are compressed and held together by coarse fibrous strands. *D*, section of tissue obtained four weeks after the injection of Carabba's solution. This section shows coarse bundles of fibrous tissue adjacent to muscle, which are more mature than those in section *C*. *E*, section of tissue obtained eight weeks after the injection of Carabba's solution. A dense firm adult fibrous tissue is present.

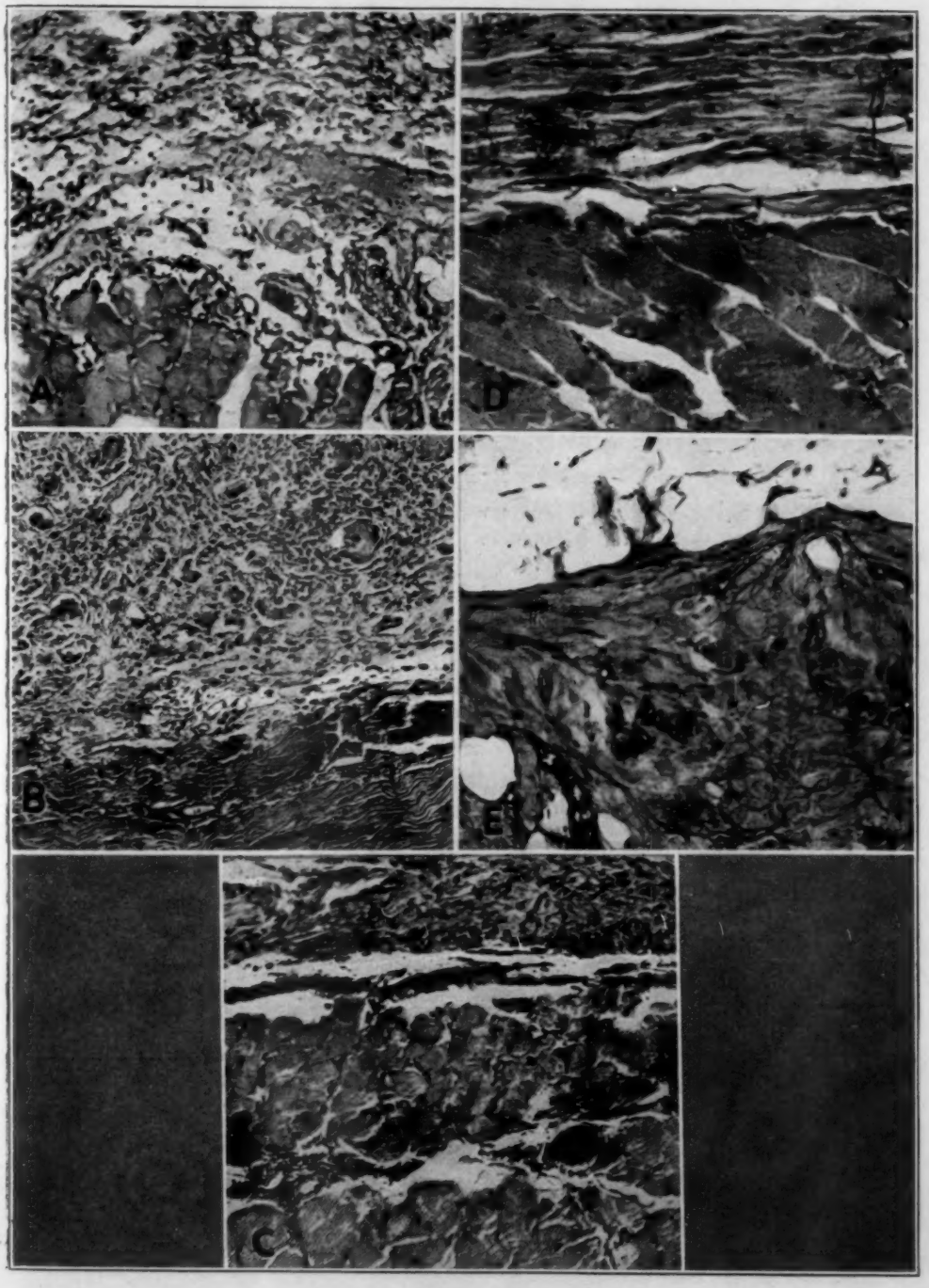

Figure 5

The animals were killed at intervals of one hour, twenty-four hours, three days, seven days, two weeks, three weeks, four weeks, six weeks and eight weeks, and sections obtained from the sites of injection were studied. In addition, four rats were given injections intraperitoneally of galtanol, sodium psylliate, a solution of iodine and tannic acid and Carabba's solution, and sections were made in forty-eight hours to note the peritoneal reaction and the effect on the abdominal contents.

Tissue from the sites of the injection was excised, fixed in formaldehyde, embedded in paraffin, cut in longitudinal sections and stained with hematoxylin and eosin for microscopic study, and in addition some sections were stained with the triple Mallory stain, the silver method of Foot and Foot and the Van Gieson stain for the connective tissue reaction.

RESULTS

Because the reactions induced by each sclerosing solution were so nearly similar, I have grouped the typical reactions at the different time intervals and noted the individual variations. A complete analysis of reactions to each solution is given in tables 1 to 6. In table 7 is presented a summation of the histologic changes with all the solutions.

Sections obtained one hour after injection showed a slight cellular reaction of polymorphonuclear leukocytes, a few lymphocytes and histiocytes and occasional fibroblasts. The tissue into which the modification of Mayer's solution was injected showed severe necrosis of the muscle.

Sections obtained twenty-four hours after injection showed slight edema of the injured area with marked exudation of polymorphonuclear leukocytes. A few lymphocytes and histiocytes and a moderate number of fibroblasts were present. The tissue into which the modification of Mayer's solution was injected showed the maximum amount of necrosis of the muscle, and in that into which the iodine and tannic acid solution was injected there was a small abscess, which did not contain any microorganisms.

Sections obtained three days after injection showed that the proliferation of fibroblasts was predominant, with many wandering phagocytes and some lymphocytes. There were few polymorphonuclear cells. Necrosis of the muscle was still most evident in the tissue into which the modification of Mayer's solution was injected.

Sections obtained seven days after injection showed early fibrosis with all solutions. The fibroblasts were much denser, and fibrils could be made out between them. Many histiocytes and a few lymphocytes were present. Only the tissue into which Carabba's solution was injected showed a few multinucleated giant cells.

Sections obtained two weeks after injection had coarser and denser fibrous tissue separating the more mature fibroblasts. Many wandering phagocytes were still present, and in the tissue into which galtanol and the modification of Mayer's solution were injected there were many multinucleated giant cells.

Sections obtained three weeks after injection showed a more mature fibrous tissue with occasional wandering phagocytes. In the tissue into which galtanol was injected there were many giant cells and also a few lymphocytes.

TABLE 1.—*Histologic Changes Produced by Galtanol* *

	1 Hr.	24 Hr.	3 Days	7 Days	2 Wk.	3 Wk.	4 Wk.	6 Wk.	8 Wk.
Necrosis	+	+	+	0	0	0	0	0	0
Lymphocytes	+	+	0	+	+	0	0	0	0
Leukocytes	0	+++	0	0	0	0	0	0	0
Histiocytes	+	+	++	++	++	++	0	0	0
Fibroblasts	0	+	++	+++	+++	+++	++	++	++
Giant cells	0	0	0	0	++	+	++	++	++
Fibrosis	0	0	0	+	++	+++	+++	+++	++++

* The plus signs in this and the following tables indicate the degree of reaction in the tissues with the different solutions; 0, indicates no change and 4 plus indicates a very marked change.

TABLE 2.—*Histologic Changes Produced by Sodium Psylliate*

	1 Hr.	24 Hr.	3 Days	7 Days	2 Wk.	3 Wk.	4 Wk.	6 Wk.	8 Wk.
Necrosis	+	+	+	0	+	+	0	0	0
Lymphocytes	+	++	+	++	0	0	+	0	0
Leukocytes	0	+++	0	0	0	0	0	0	0
Histiocytes	+	++	+	++	++	+++	+	0	0
Fibroblasts	0	++	+++	+++	++++	++++	+++	0	0
Giant cells	0	0	0	0	0	0	0	0	0
Fibrosis	0	0	+	++	++	+++	+++	++++	++++

TABLE 3.—*Histologic Changes Produced by Bratrud's Solution*

	1 Hr.	24 Hr.	3 Days	7 Days	2 Wk.	3 Wk.	4 Wk.	6 Wk.	8 Wk.
Necrosis	+	+	0	+	+	+	0	0	0
Lymphocytes	++	0	0	++	++	0	++	0	0
Leukocytes	+	+++	+	0	0	0	0	0	0
Histiocytes	0	++	+++	++	+	0	+	+	0
Fibroblasts	+	+	++	++++	++++	++	++	++	0
Giant cells	0	0	0	0	++	0	0	0	0
Fibrosis	0	0	0	0	+++	++++	++++	+++	++++

TABLE 4.—*Histologic Changes Produced by a Modification of Mayer's Solution*

	1 Hr.	24 Hr.	3 Days	7 Days	2 Wk.	3 Wk.	4 Wk.	6 Wk.	8 Wk.
Necrosis	+++	+++	+++	0	0	0	0	0	0
Lymphocytes	+	0	+++	0	0	+	++	0	0
Leukocytes	0	++	+	0	0	0	0	0	0
Histiocytes	+	0	++	+++	0	+	++	0	0
Fibroblasts	+	++	++	++	+++	+++	+++	0	0
Giant cells	0	0	0	0	0	0	++++	0	0
Fibrosis	0	0	0	0	+++	++++	++++	++++	++++

Sections obtained four weeks after injection showed more mature fibrous tissue; occasional wandering leukocytes and lymphocytes were present. Tissue into which galtanol was injected still showed many multinucleated giant cells filled with brownish granules. Tissue into

which the modification of Mayer's solution was injected showed many giant cells.

Sections obtained six weeks after injection showed fibroblastic tissue similar to that seen in the sections obtained at four weeks. Tissue into which galtanol was injected still showed many foreign body giant cells filled with brownish granules.

TABLE 5.—*Histologic Changes Produced by Tannic Acid Solution*

	1 Hr.	24 Hr.	3 Days	7 Days	2 Wk.	3 Wk.	4 Wk.	6 Wk.	8 Wk.
Necrosis	+	0	+	0	0	0	0	0	0
Lymphocytes	++	++	0	+	++	0	+	0	0
Leukocytes	++	++++	++	0	0	0	0	0	0
Histiocytes	+	+	++	0	+	+	++	0	0
Fibroblasts	0	++	++	+++	++++	+++	+++	++	0
Giant cells	0	0	0	0	0	0	0	0	0
Fibrosis	0	0	0	++	++	+++	+++	+++	++++

TABLE 6.—*Histologic Changes Produced by Carabba's Solution*

	1 Hr.	24 Hr.	3 Days	7 Days	2 Wk.	3 Wk.	4 Wk.	6 Wk.	8 Wk.
Necrosis	++	+	++	++	+	0	0	0	0
Lymphocytes	+	+	++	0	0	0	0	0	0
Leukocytes	+	+++	0	0	0	0	0	0	0
Histiocytes	+	++	++	++	0	+	0	0	0
Fibroblasts	0	++	+++	+++	+++	0	+	0	0
Giant cells	0	0	0	+++	0	0	0	0	0
Fibrosis	0	0	+	+	+++	+++	+++	++++	++++

TABLE 7.—*Summation of Histologic Changes Produced by Sclerosing Solutions*

	Necrosis	Acute Inflammation	Early Repair	Late Repair	Fibrosis	Fibroblastic Reaction
Galtanol	+ 3 days	+++ 1 day	++ 3-7 days	+++ 2-3 wk.	++++ 3-8 wk.	++ 2-8 wk.
Sodium psylliate	+ 3 wk.	+++ 1 day	+++ 3-7 days	++++ 2-4 wk.	++++ 1-8 wk.	0
Bratrud's solution	+ 3 wk.	+++ 1 day	++++ 3-7 days	++++ 1-4 wk.	++++ 1-8 wk.	± 2 wk.
Modification of Mayer's solution	+++ 3 days	++ 1 day	++ 3-7 days	+++ 2-4 wk.	++++ 2-8 wk.	++++ 4 wk.
Tannic acid solution	± 3 days	++++ 1-3 days	++ 3-7 days	+++—++++ 2-4 wk.	++++ 1-8 wk.	0
Carabba's solution	++ 2 wk.	+++ 1 day	+++ 3-7 days	+++ 1-2 wk.	++++ 2-8 wk.	+ 1 wk.

Sections obtained eight weeks after injection all showed a dense fibrous tissue, except the tissue into which galtanol was injected, which still had many giant cells in one area.

The sections stained with the silver method of Foot and Foot showed many fine argyrophilic fibers in the reticulum among the collagen fibers at the seven day period, which were gradually and completely replaced by dense collagen at the eight week period.

The animals into which Bratrud's solution and the modification of Mayer's solution were injected were the only ones to show a systemic reaction of mild to severe shock, and a few died within one hour, when the dose was larger in the earlier part of the experiment.

Animals given intraperitoneal injections of galtanol, Bratrud's solution, a solution of iodine and tannic acid and Carabba's solution had a very mild reaction. There was no macroscopic peritoneal reaction in the sections cut at the end of forty-eight hours. There was no plastic exudate or free fluid in the abdominal cavities. Microscopically, sections of peritoneum and muscle showed a moderate amount of fibrinous plastic exudate in which were many polymorphonuclears, wandering phagocytes and several fibroblasts. A few lymphocytes could also be made out.

COMMENT

Chemical irritation of tissue will produce an inflammatory exudative reaction. The purpose of this exudate is to neutralize and overcome the irritant and remove it. Attempts at repair may begin early in the process and may be enhanced or retarded by the persistence of the irritant solution. An excessive mass of fibrous tissue may be produced to fill the gap by repeated frustration of healing. This is brought about by renewing the irritation of the repairing tissue itself, so that layer after layer of this new tissue is laid down and consolidated into a firm scar. It is readily seen that if this process is kept up for a long time the formation of a great quantity of scar tissue would result.

While at first connective tissue cells lie loosely about so that spaces between them accommodate fluid and wandering cells, they later produce in the marginal parts of their cytoplasm the fibrils which stain differently from the general protoplasm and which, increasing in number and in thickness, become arranged in roughly parallel form so as to produce a dense fabric in which the cells themselves finally become rather inconspicuous. This microscopic sequence may then be explained as argyrophil or reticulum fibril formation in a homogeneous collagen matrix. In a later period of scar tissue formation, the collagen does not impregnate with silver stain. This process so carefully studied by Minnervini,[15] Maximow,[16] Wolbach,[17] Mallory and Parker,[18] Foot [19] and many others constitutes the formation of scar tissue.

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The results in this experimental work obtained with the aforementioned sclerosing solutions well demonstrate these tissue changes. All solutions except the iodine and tannic acid solution elicited a mild inflammatory exudative reaction up to twenty-four hours with a marked subsidence at the three day period. With the iodine and tannic acid solution an abscess was evident at the twenty-four hour period. The reaction to all the solutions at the end of the seven day interval consisted chiefly of a proliferation of fibroblasts with early repair. At later periods, from two to eight weeks, the young fibroblasts could be seen undergoing changes of maturity, becoming smaller and more elongated, and the argyrophilic reticulum fibrils between them were condensed and supplanted by firm collagenous tissue. The modification of Mayer's solution was the only solution to produce marked necrosis of muscle up to three days, while the necrosis of muscle produced by Carabba's solution was moderate up to seven days. The foreign body reaction to galtanol persisted for from two to eight weeks. This indicates the failure of the tissues to get rid of the residual iritant solution, and while it may continue the proliferation of connective tissue, a possible danger lies in the formation of a foreign body granuloma.

It has not as yet been determined which constituents of each solution have a stimulating effect on the proliferation of new connective tissue. This problem is under consideration and will ascertain the rationale for using the various ingredients of each solution.

SUMMARY

In a series of rats sclerosing solutions were injected into the muscles of the anterior abdominal wall on each side. Six different solutions were used: (1) galtanol, (2) sodium psylliate, (3) Bratrud's solution, (4) a modification of Mayer's solution, (5) iodine and tannic acid solution and (6) Carabba's solution. Biopsy specimens were obtained from the sites of injection at intervals of one hour, twenty-four hours, three days, seven days, two weeks, three weeks, four weeks, six weeks and eight weeks. Intraperitoneal injections were made with galtanol, sodium psylliate, iodine and tannic acid solution and Carabba's solutions, and the animals were examined in forty-eight hours.

There was a slight necrosis of muscle, except when modification of Mayer's solution was used, and then it was marked. The inflammatory exudation was mild, reaching its peak at twenty-four hours and then subsiding completely in the next forty-eight hours. Iodine and tannic acid solution was the only one to produce abscess formation at the end of the twenty-four hour interval. Proliferation of fibroblasts became predominant at three days, and at seven days there was some evidence of new collagenous tissue with dense fibrous tissue at eight

weeks. Foreign body giant cells were present in the tissue into which galtanol was injected throughout the period between two and eight weeks; they were present in the tissue into which Bratrud's solution was injected at two weeks only, in that into which the modification of Mayer's solution was injected at four weeks only and in that into which Carabba's solution was injected at seven days only.

The only solutions that produced a systemic reaction were Bratrud's and the modification of Mayer's solutions.

After intraperitoneal injection of galtanol, sodium psylliate, iodine and tannic acid solution and Carabba's solution no gross signs of inflammatory exudate were evident at forty-eight hours, but microscopically there was a moderate inflammatory reaction with many polymorphonuclears, wandering macrophages, few lymphocytes and many fibroblasts.

CONCLUSION

The injection of certain sclerosing solutions into the abdominal muscle of rats produced firm scar tissue in eight weeks.

The persistence of foreign body giant cells from two to eight weeks after the injection of galtanol is noted, and it is suggested that its clinical use may be unfavorable.

The systemic reaction following the injection of Bratrud's solution and of a modification of Mayer's solution as well as the marked necrosis of muscle following the injection of the latter makes them unsatisfactory.

The iodine and tannic acid solution, although producing marked fibrosis in the later stages, should be carefully investigated clinically because of the abscess formation noted in the twenty-four hour section.

With Carabba's solution there were mild necrosis of muscle and a foreign body giant cell reaction in the seven day section only. This solution may be satisfactory for clinical use in proper doses.

Finally, sodium psylliate seems to have the necessary qualifications for a safe and satisfactory sclerosing irritant in the formation of scar tissue. It produces a mild inflammatory reaction, slight necrosis of muscle in early stages, no systemic reaction when injected intramuscularly and moderate reaction on intraperitoneal injection. It produces firm scar tissue without any undesirable histologic changes.

PERITONITIS

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ANATOMY AND HISTOLOGY

The peritoneum is the largest serous membrane in the body. Hertzler[1] measured the peritoneal and the cutaneous surfaces of twenty cadavers and found that the average of the measurements for the former was 3,268 square inches and for the latter, 3,436 square inches. Thus the opinion usually held that the surface area of the peritoneum is about equivalent to the cutaneous surface area of the body is approximately correct.

A part of the peritoneum is applied to the abdominal wall, the remainder being reflected over the viscera contained in the peritoneal cavity. In the male the peritoneum is a closed sac, but in the female the free ends of the fallopian tubes open directly into the peritoneal cavity. The surface of the peritoneum is covered with flattened cells which are variously called epithelium, endothelium or mesothelium. According to Jordan,[2] these cells are mesothelium. They are sometimes known as squamous epithelium. Maximow refers to the cell layer covering the surface of all serous membranes as mesothelium. However, reference to the superficial cells of these serous membranes as endothelium is usual in clinical descriptions and will be adhered to here.

The endothelial cells of the peritoneum have undulating margins, the corners being frequently pushed between the sides of adjoining cells. This irregularity may be accentuated by contraction or by successive contraction and expansion, particularly on the under-surface of the diaphragm. The endothelium of the peritoneum differs in its form from the endothelium lining the blood and lymph vessels, the latter being usually arranged with the long axis of its cells parallel with the axis of the vessel, and the cells are elliptoid in shape and more irregular in outline and in size than the peritoneal cells. The cells of the peritoneum are quite flat and have ovoid nuclei. In staining, they may group themselves in such a manner as to suggest stomas or stigmas.

The DaCosta Foundation Oration, read before the Philadelphia County Medical Society, Philadelphia, April 14, 1937.

1. Hertzler, A. E.: The Peritoneum, St. Louis, C. V. Mosby Company, 1919, vol. 1.

2. Jordan, H. E.: A Text Book of Histology, New York, D. Appleton-Century Company, Inc., 1934.

However, these openings, formerly supposed to afford an exit for the exudate of the peritoneum, have been proved to be artefacts in the staining and do not actually exist. The nucleus is usually situated about the center of the cell but may be eccentric; the long axis corresponds to the long axis of the cell. There may be two nuclei in a cell. The cytoplasm of the cell in the fresh stage is transparent.

Though some authorites have described cilia on the parietal peritoneum, Hertzler [1] seems to have demonstrated that these so-called cilia were merely deposits of fibrin from the coagulation of fluid normally covering the cells. The cells are held together by an intercellular substance, which was thought by some to be lymph between the cells but has been more generally accepted as an intercellular cement which is different from the fluid in the lymph vessels. If the intercellular connection between the cells is broken and the substance beneath the cells is permitted to come in contact with the blood, coagulation occurs.

The pits in the peritoneum that lines the diaphragm are doubtless caused by folds in the peritoneum and may disappear when the peritoneum is carefully stretched. There seems to be no essential difference between the peritoneum that lines the diaphragm and that elsewhere in the abdominal cavity.

The discredited stigmas and stomas were formerly the basis of false theories as to absorption from the peritoneum. As they were supposed to be far more abundant on the under-surface of the diaphragm than elsewhere, it was assumed that absorption from the peritoneum of the diaphragm was particularly rapid. It is generally accepted now, however, that this is not true and that the capacity for absorption from the peritoneum, so far as its histologic structure is concerned, is about the same everywhere. One of the reasons given for the treatment of peritonitis by placing the patient in a sitting position was that by gravity the peritoneal exudate should be directed away from the diaphragm, where absorption through the stigmas and stomas was rapid. When fluid was given intraperitoneally for absorption, such as salt solution, the patient was often placed in the Trendelenburg position, thus bringing the fluid more in contact with the under-surface of the diaphragm. The upright position has proved of value in the treatment of peritonitis chiefly because the exudate may be gathered into one small portion of the peritoneum, i. e., in the pelvis, where it can be more readily removed and will have a smaller area for absorption than if smeared over the whole peritoneal surface. Then, too, it is probable that even though the diaphragmatic peritoneum has no more capacity for absorption than the peritoneum elsewhere, the movements of respiration—the contraction and relaxation of the diaphragm with the liver beneath it—may

act somewhat as a pump and mechanically force exudate into the peritoneum more rapidly than it would be absorbed without such alternate compression and relaxation.

Beneath the layer of endothelial cells is a basement membrane, made up of connective tissue fibrils arranged in parallel bundles and bound together with a cement substance. The cement substance appears not only to hold the connective tissue fibrils of the basement membrane together but to keep the endothelial cells in place much as tiles would be held by cement beneath them. In irritation of the peritoneum an excessive amount of cement substance is apparently one of the first products of peritoneal exudation, as it emitted between the cells and presents a fibrinous discharge.

Beneath this basement membrane is a layer of loose connective tissue, through which course blood and lymph vessels. In regions where the peritoneum is less mobile than others, as over the bands of the colon, the central tendon of the diaphragm and over the liver and spleen, there is a small amount of connective tissue. The connective tissue in other regions, such as the parietal peritoneum, is more abundant and frequently contains much fat.

The blood vessels of the peritoneum may be divided into those that can be seen under normal conditions and those that are not visible. The latter are doubtless abundant not only in the peritoneum but in other tissues of the body and are called by Hertzler potential vessels. Ordinarily these small vessels do not contain red blood cells and are invisible. They probably transport serum, and possibly some white blood cells may make their way through them. In the presence of irritation they quickly dilate and become active with circulating blood. It is these vessels that under the sudden stimulus of irritation or inflammation provide the diffuse redness of the peritoneum. They can be demonstrated experimentally by the injection of a solution of silver nitrate and appear under the microscope to divide the peritoneum into quadrilateral areas. They arise at right angles from the visible vessels. They are separated from the endothelial cells only by their lining and a basement membrane.

The lymphatics of the peritoneum lie in the same stratum of connective tisue in which the blood vessels are found, only probably somewhat deeper. They form a network of relatively large vessels, irregular in size. The large lymph channels are connected by fine canals, but there seems to be no organic connection with the blood vessels or with the connective tissue spaces. The lymph channels are apparently a closed system, just as the blood vessels are, and interchange with the connective tissue spaces is doubtless a chemical process and does not involve an actual mechanical connection with the special spaces. Lymph vessels

of the peritoneum are uniformly distributed, and the peritoneum of the diaphragm probably possesses no more abundant lymphatics than the peritoneum elsewhere. The lymphatics of the diaphragm doubtless communicate with the thoracic lymphatics, though the communication is by ordinary channels and not through any special perforations, as has been sometimes assumed. One would no more speak of communication of these lymphatics in this manner than one would speak of perforation of the arteries and veins in the intestinal wall. Lymphatic currents from the peritoneum over the diaphragm lead into the lymph nodes of the mediastinum and not to the pleural surface.

PHYSIOLOGY

One of the most interesting features of the physiology of the peritoneum is the method of absorption. There has been much discussion about this, and it may not now be considered completely settled. Undoubtedly absorption occurs both through the lymph vessels and through the blood vessels, but probably it is much greater through the latter. The lymphatic duct is primarily a collector of material from the intestinal lacteals and carries nutrient material, while the lymphatics of the peritoneum itself empty into the lymph nodes and not directly into the thoracic duct as the lacteals do. Carcinoma of the thoracic duct is an extremely rare lesion, whereas it is well known that metastatic cancer following the lymphatic route out of the abdomen commonly travels along the lymphatics of the mediastinum.

The rate of absorption from the peritoneal cavity varies greatly according to the character and the concentration of the fluid as well as the pressure that is maintained. The absorption of hypotonic solutions is rapid at first. Afterward, as osmotic equilibrium is established, the absorption becomes slower.

The phagocytic cells, the polymorphonuclears and large mononuclears, engulf much of small particulate matter placed in the peritoneal cavity, and absorption of these particles is largely by the blood stream. According to Hertzler,[3] who has done such excellent work on the peritoneum, after small foreign bodies are introduced into the peritoneal cavity there is first a contraction of the vessels of the peritoneum, soon followed by dilatation. With the dilatation there is increased exudation into the peritoneum, which sweeps the particles toward the nooks and the dependent portions of the peritoneal cavity and around the great omentum. This may occur in any direction. The great omentum and the region around the roots of the mesentery are usually the centers of the greatest accumulation, but the material may be deposited

3. Hertzler, A. E.: (*a*) Surgical Pathology of the Peritoneum, Philadelphia, J. B. Lippincott Company, 1935; (*b*) footnote 1.

anywhere. When these particles are located, plastic exudation throws up a granular mass, and they are often encapsulated. This requires two or three hours and may result in a permanent resting place of the foreign particles in the peritoneum somewhat similar to what is observed with granules of soot in the lungs or powder stains in the skin. Some of the particles gain access to the lymph nodes. The number of cells in the peritoneal fluid is increased, the cells coming from the points of greatest irritation in the peritoneum. These cells form a new peritoneum around the capsules of the foreign bodies when they are surrounded by the cells. At first polymorphonuclears predominate, but later mononuclears take part in this process. Phagocytic cells may surround the small particles and carry them to the lymph nodes, or they may, according to Hertzler,[3] break up the foreign body, destroying themselves at the same time. However, if the particles are soluble, such as particles of fibrin, the cells usually remain alive. Very small particles of lampblack introduced into the peritoneal cavity are doubtless disposed of in part by being carried into the circulating blood, and the larger particles are surrounded by a cell or cells and may be carried to the lymph nodes or encapsulated.

Defibrinated blood is rapidly absorbed from the peritoneum, but coagulated or whole blood is absorbed much more slowly. According to Jordan,[4] Shipley and Cunningham[5] and others, the chief agents in disposing of clots are the monocytes (macrophages), which carry the débris both to the blood and to the lymph capillaries of the peritoneum. Bacteria are disposed of in the same manner.

Absorption is hastened by many things, among others by massage. The action of the diaphragm tends to promote absorption from the peritoneum in the upper part of the abdominal cavity. Slowing of absorption may be caused by abundant fibrinous exudate, especially in walled-off cavities.

The increase in intra-abdominal pressure hastens absorption from the peritoneum so long as the increase is not sufficient to retard the returning flow of blood. After this point the increased pressure tends to delay absorption.

The omentum usually has an active function in inflammation of the peritoneum. Its protective influence in attempting to wall off inflam-

4. Jordan, H. E.: Personal communication to the author. Jordan, H. E., and Speidel, C. C.: Studies on Lymphocytes: I. Effect of Splenectomy, Experimental Hemorrhage and a Haemolytic Toxin in the Frog, Am. J. Anat. **32**:155 (Sept.) 1923; The Behavior of the Leukocytes During Coincident Regeneration and Thyroid-Induced Metamorphosis in the Frog Larva, with a Consideration of Growth Factors, J. Exper. Med. **40**:1 (July) 1924.

5. Shipley, P. G., and Cunningham, R. S.: Studies on Absorption from the Serous Cavities, Anat. Rec. **2**:181, 1916.

matory areas and prevent the extension of peritonitis is well known. That the omentum can absorb is undoubtedly true, as can be readily demonstrated by placing the omentum of an experimental animal in a vessel containg a solution of some drug, such as strychnine. The absorption of fluids by the omentum is through the blood vessels.

Sappay and Ranvier [6] do not believe that the great omentum has lymphatics. Casparis,[7] however, seems to have demonstrated lymphatics in the great omentum which communicate with the lymph glands at the greater curvature of the stomach. In a recent study of the omentum, Simer [8] stated:

> Contrary to the generally accepted belief, and to the frequent statements in the literature, the adult human omentum is provided with lymphatic vessels which accompany the haemal channels, and, judging from the large number of valves present, are of great importance in the physiology of this organ. The findings in the adult rat are the same.

When the peritoneum is inflamed, its sensitiveness is greatly increased. The parietal peritoneum is supplied by branches from the spinal nerves as well as by the sympathetic nerves, while the visceral peritoneum has chiefly, if not only, the sympathetic nerves. Nerves have not been satisfactorily demonstrated in the omentum. Simple hyperemia does not increase the sensitiveness of the peritoneum unless there is exudate. The presence of exudate heightens the sensitiveness of the peritoneum.

Absorption from the inflamed peritoneum seems to be about the same as from the normal peritoneum. Small particles are absorbed not only into the anterior mediastinal lymph nodes, which receive most of the particles of the peritoneum, but into the anterior and posterior lumbar lymph nodes, which also receive some of the material. There is little drainage of the peritoneum by the thoracic duct.

PERITONEAL REPAIR

If the peritoneum is injured mechanically or chemically or by bacteria, there is usually an attempt at repair. The most common mechanical injury is that inflicted by any abdominal operation, and the process of repair, as in wounds in other tissues, depends largely on whether there is infection by bacteria or whether repair occurs under aseptic conditions.

Primary repair in all injured tissues takes place by means of connective tissue, though less connective tissue develops in primary than

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6. Sappay and Ranvier, cited by Hertzler.[1]
7. Casparis, H. R.: Lymphatics of the Omentum, Anat. Rec. **15**:93, 1918.
8. Simer, Parke H.: On the Morphology of the Omentum, with Especial Reference to Its Lymphatics, Am. J. Anat. **54**:203 (March) 1934.

in secondary repair. More highly differentiated repair usually follows primary repair, but the first bond in holding the injured tissues together, aside from temporary agglutination by exudate, is connective tissue.

In some excellent experimental work, Hertzler [3] seems to have shown that in the healing of peritoneal wounds under optimum conditions without bacterial infection, unusual trauma or the presence of blood clots, a clear structureless exudate is thrown down a few minutes after the peritoneal surfaces are approximated with fine silk sutures. Within ten minutes bundles of fibrin extend from one surface of the peritoneum to the other, and within a few hours the bundles are fully developed. Usually there is a subperitoneal edema, which elevates the serous surfaces and brings them closer together. The bundles of fibrin contract as they mature. These primary bundles of fibrin remain in position under aseptic conditions and gradually form *directly* fibrous tissue without any replacement. These changes begin about the third or fourth day, and by the sixth or eighth day the bundles of fibrin are *directly* converted into adult connective tissue bundles. Cells may invade the interstices between the bundles, but they do not replace them. These bridges of fibrin connective tissue are covered with endothelium, not from the adjacent margins of the endothelium, according to Hertzler, but with endothelium formed from monocytes, wandering cells or clasmatocytes which spread over the surface and flatten out. In this way there is complete endothelization in a week or ten days. This favorable process, however, may be interrupted by sepsis, by undue trauma of the tissues or by digestive juices on the peritoneal surface. Constitutional conditions, such as intense jaundice, may also affect such healing.

The muscular and mucous layers of the apposed bowel require several weeks for healing, but the important surgical feature is the prompt union of the peritoneal surfaces. If conditions are not satisfactory for primary healing, secondary union may occur. Here there is agglutination of the surfaces from a granular mass of exudate, which sooner or later is absorbed. This exudate consists of granular débris with exudate from the peritoneal surfaces. Granulation tissue is formed and then come fibroblasts, from which connective tissue develops.

Aseptic irritation of the peritoneal cavity may cause adhesions, which may be temporary or permanent. With infection, there is an outflow of serum which infiltrates the connective tissue spaces and forms exudate on the surfaces where the tissues are infiltrated with leukocytes. Hyperemia occurs with leukocytic infiltration of the connective tissue around the blood vessels, and then there is migration of the omentum to the site of infection, probably by some cellular mass attraction similar to chemotaxis. The surfaces of the organs are covered with exudate

and held together by a kind of granular fibrin. The connective tissue fibrin does not form because the bacterial toxins prevent, but the granular fibrin surrounds the affected peritoneal surfaces and frequently serves to prevent the infection from spreading. This may produce temporary adhesions, which are absorbed sometimes after several months. If the infection is marked, it may cause sufficient reaction for a deposit of a different type of fibrin along the outer margins of this granular fibrin, and from this permanent adhesions may form. Gonococci are great fibrin producers, and from this type of fibrin permanent adhesions often result.

When these temporary adhesions form about an infected area, the bowel is infiltrated, and the tissues, especially connective tissue, become very friable, so the bowel can be injured readily or perforated by traction or manipulation which would not affect a normal intestine. If the peritoneum is exposed or continuously irritated for a long time, the fibrin is invaded with leukocytes, and granulation tissue is formed from which connective tissue develops, as in healing by second intention.

PATHOLOGIC PICTURE OF ACUTE PERITONITIS

Acute peritonitis may be divided into three stages from a pathologic point of view: the hyperemic, the exudative and the plastic stage.

In the first stage of peritonitis there is hyperemia. The potential vessels which have been described rather suddenly dilate, and this produces a pinkish blush on the peritoneal surface. Normally these vessels are empty of red cells and are invisible. What was formerly considered an escape of leukocytes from the vessels in the early stages of inflammation is probably dilatation and filling of these potential vessels with blood. The circulation is at first speeded up as the vessels dilate, and then as the white corpuscles adhere to the wall of the vessel the circulation is somewhat slowed. Later leukocytes and also serum escape from the vessels into the surrounding tissue. The potential vessels have no wall except the endothelial lining with its basement membrane. The surrounding lymph vessels contain lymph and many leukocytes. As the integrity of the walls of the vessels becomes impaired, the red cells escape into the surrounding tissue and exudate is quickly thrown off on the surface, though the endothelial cells are preserved for a while. The mononuclear cells penetrate the basement membrane, and later endothelial cells are replaced by polymorphonuclear cells and fibrin. The basement membrane is held together.

The hyperemic stage, which has just been described, is probably common to the different types of peritonitis, even to the aseptic form. Hyperemia and dilatation of the mesenteric and peritoneal vessels may often accompany other conditions besides peritonitis, particularly when

there is intestinal obstruction. In inflammation, however, the diffuse redness, which has been mentioned as an early stage caused by dilatation of the potential vessels, is always a distinct feature, though dilated vessels without this diffuse redness may occur around the margin of the peritonitis or may be an accompaniment of some other condition, such as obstruction. The hyperemic stage of peritonitis occurs early, within the first hour after perforation of a duodenal ulcer, for instance. The distal loops of bowel may show only dilatation of normal or service vessels, whereas those nearest the site of a perforation will have the diffuse redness. The abdominal wall usually shares in these vascular changes, hyperemia of the parietal peritoneum taking place. Even when the hyperemia is slight, there may be a loss of the glistening surface of the normal peritoneum. When hyperemia is marked, there is an escape of red cells outside of the blood vessels which causes dark areas within the peritoneal surface, even when there is no exudate. This shows an intense irritation.

The exudative stage is a rapid sequel to the hyperemic stage. Serum and cells are found about the walls of the blood vessels in the subperitoneal tissue and on the surface of the peritoneum. This exudate is probably protective and forms adhesions to the adjacent structures, so that the inflammatory process will not extend into the general peritoneal cavity. The peritoneum is always thickened with edema, which elevates it. In the exudative stage the appearance of the peritoneum is significant. If the exudate is pink or reddish, it shows a formation of a granulation fibrin and good defense; if it is whitish and smooth, it indicates that fibrin and protective adhesions are not being formed, and the prognosis is grave. The adherent tissues here are easily separated, and infection will break down the feeble barriers. As the disease progresses, there may be numerous areas which are walled off.

In the plastic stage the exudate forms adhesions and joins the peritoneal surfaces together, so walling in the affected area and protecting the peritoneal cavity. The surfaces of the peritoneum are fused together by this material in the exudative stage. If these areas are separated, a sheetlike exudate is found which is made up of granular fibrin and remains attached to the peritoneal surface. Occasionally the exudate covers wide areas. The exudate sometimes becomes vascularized as true granulation tissue. This is chiefly found when the peritoneal surface is long exposed or when there is prolonged contact with a drain, especially a gauze drain. The plastic exudate may be without structure and whitish or grayish. This shows a lack of reaction and is ominous. It is the type of exudate usually found at necropsy.

These changes do not necessarily succeed each other in the order named. Hyperemia occurs first; then exudation occurs, and plastic

exudation may follow while the peritonitis is extending to other points with new areas of hyperemia. Areas of peritonitis may disclose all three stages of peritonitis. The exudate of serum and leukocytes and finally an escape of red cells may be more pronounced in some places than in others. The flocculent exudate of imperfect adhesions is made up of granular fibrin with degenerated cells.

In cases of acute peritonitis the deeper layers of the bowel may not show much change, but when peritonitis runs a slower course the muscle wall of the bowel will show degenerative changes, and when the peritonitis is localized the connective tissue becomes friable, as in a walled-off abscess. In this type of peritonitis the adhesions are usually temporary and, if the patient recovers, are removed sooner or later by the phagocytes.

There are many unusual forms of peritonitis, some of which will be discussed later.

Rheumatic peritonitis, which Hertzler [9] considered a form of aseptic peritonitis, occurs associated with some forms of rheumatism. Cases of peritoneal actinomycosis occur. Wetherell [10] described cases in which pseudoperitonitis resulted from injuries to the back and from neurologic conditions. Peritonitis has occurred in cases of tularemia, and Abt [11] has reported fetal peritonitis.

Peritonitis may occur in the absence of bacteria, as around strangulated tissue before bacteria penetrate. The localized foci of peritonitis that are commonly found around the gallbladder before the bacteria have penetrated are indirectly caused from infection and arise from contact with toxins and infiltrating products before the bacteria have reached the peritoneal cavity. Almost any chemical that is introduced into the peritoneal cavity will produce a limited form of peritonitis. If a sufficient amount is introduced, more extensive irritation and a shock-like conditon may occur.

Clinically, puerperal peritonitis is much like the peritonitis that arises from lesions of the gastro-intestinal tract. Doubtless many cases of puerperal peritonitis are due to infection from the anal region that is carried into the vagina by uncleanly methods, so that bacteriologically this form of peritonitis may resemble that which follows a ruptured appendix. Often, however, streptococci seem to dominate, and the condition may develop into progressive fulminating peritonitis of the virulent type. With more careful obstetric aseptic management, such cases are becoming rarer.

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9. Hertzler,[1] vol. 2; footnote 3a.

10. Wetherell, F. S.: Pseudoperitonitis Due to External Traumatism, Am. J. Surg. **9**:480 (Sept.) 1930.

11. Abt, I. A.: Fetal Peritonitis, M. Clin. North America **15**:611 (Nov.) 1931.

SYMPTOMS OF ACUTE PERITONITIS

When acute peritonitis is spoken of it is usually a type of septic peritonitis that springs from lesions of the gastro-intestinal tract.

The symptoms of acute peritonitis may vary considerably. In a typical case pain is the first symptom. This may be due to spasm or to exudation into a viscus together with hyperemia, which permits the transmission of pain from the sympathetic nerves. The methods of transmitting pain from the peritoneal cavity have undergone considerable discussion and cannot be dealt with here at length. Years ago Lennander claimed that the viscera of the peritoneal cavity were devoid of any sensation. It seems to be proved now, however, that the sympathetic system can transmit certain types of pain, and this can be excited largely by tension within the tissue or by spasmodic contraction of the muscle. Soon after this occurs, however, the parietal peritoneum becomes affected, and the pain is then transmitted by cerebrospinal nerves. The pain usually originates from the sympathetic nerves, being transmitted to the ganglions, and is often complained of first in the epigastrium, but in a few hours it occurs at the site of the lesion. The pain caused by established peritonitis is transmitted by the cerebrospinal nerves. It is increased by the movement of inflamed surfaces on each other, so that pressure on the abdomen which brings the inflamed surfaces together increases the pain and tenderness. After adhesions have occurred, the pain is frequently lessened, because the inflamed parts are somewhat splinted together by adhesions. Muscular rigidity is one of the early symptoms of peritonitis and is doubtless a reflex, such as is described by Hilton[12] in "Rest and Pain" to protect the inflamed surface by the splintlike action of the muscles. It is most pronounced at the site of the greatest irritation and is dependent on the cerebrospinal reflex. The rupture of a hollow viscus, such as the stomach or bowel, is usually accompanied by intense abdominal pain and muscular rigidity. Often there is marked shock, soon followed by elevation of temperature and a rapid pulse.

Inflammation of a viscus that is limited to the viscus and does not involve the parietal peritoneum may not be accompanied by muscular rigidity. This occurs in certain instances in which an inflamed appendix, for instance, is in the pelvis attached to a mobile cecum and not in close proximity to the parietal peritoneum. The muscular rigidity may be lessened when the infection is walled in or the inflammation of the parietal peritoneum diminishes. As the disease advances, however, and the patient becomes more toxic, there may be some lessening of the muscular rigidity, even though the disease is progressing.

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12. Hilton, J.: Rest and Pain, edited by W. H. A. Jacobson, New York, W. Wood & Co., 1879.

One of the early striking symptoms is immobilization of the abdomen along with muscular spasm. On respiration, the abdominal muscles are fixed instead of moving synchronously.

The so-called hippocratic facies, with the face drawn and the tense, anxious expression, with dehydration apparent, occurs in the later stages of general or spreading peritonitis and is often due to dehydration from vomiting. One of the most ominous signs in spreading peritonitis is the small, thready, rapid pulse. With intravenous injections of dextrose in Ringer's solution, however, even though the patient may not recover, these features of dehydration and thready pulse are often not conspicuous.

The usual symptoms of acute infection are also present, such as nausea and often vomiting. The pulse is rapid, and the temperature is usually not high unless there has been a sudden perforation of an abscess or gangrene of the appendix. In such instances, too, a chill is not uncommon, but the chill is rarely repeated. The white blood count is elevated, usually from 12,000 to 20,000, but an extreme elevation, to 30,000 or more, may be indicative of some other lesion, particularly of pneumonia. In an exceptional case there may be but little change in the white blood count, but even here the shift to the left in the Schilling count should be present. In such cases the patient shows poor resistance. As the disease progresses, the vomiting becomes more pronounced, and often coffee-ground material is vomited from erosions in the gastric and intestinal mucosa, caused by the toxemia. This is always of serious significance. Distention occurs as the disease progresses. The distention is due to the involvement of the wall of the bowel by the inflammation of the peritoneum. If the patient survives several days, section of the wall of the bowel shows certain degeneration and weakness in the muscular coat with a fine granular change, usually seen in cases of acute degeneration, though the nerves appear to be normal.

The patient's mental condition in almost all cases of peritonitis is of interest. Usually the mind is abnormally clear and active. The patient is restless, the eyes are bright and as the disease advances he seems to be largely relieved of pain. Later there may be delirium.

Such is the clinical picture of the ordinary case of general peritonitis arising from infection of the gastro-intestinal tract. Of this, there are many variations and exceptions.

Postoperative peritonitis following leakage from an intestinal or gastric suture a few days after operation is sometimes insidious. Not infrequently there is but little muscular spasm, and the first apparent symptoms are the apprehension of the patient, an elevation of temperature and pulse rate, nausea and vomiting and some distention. If the

leakage is slow, there usually is not the pronounced classic symptom of intense pain and muscular spasm that ordinarily follows perforation of a viscus.

In the elderly person with a low resistance, the white blood count may appear to be normal. Usually there is a shift to the left of the polymorphonuclears, but even this may be comparatively insignificant. In children, too, the symptoms are often irregular.

ETIOLOGY OF SPREADING PERITONITIS

In regard to the etiology of spreading or general peritonitis, an interesting article by Pflaum [13] on "A Postmortem Analysis as to Etiology in One Thousand Cases of Peritonitis" gives much information. This report is based on 1,000 cases of peritonitis found at 14,263 necropsies in the department of pathology of the University of Minnesota from 1920 to 1932. Of these 1,000 cases, 52.5 per cent were in males, though peritonitis is supposed to be more common in the female. There were 221 cases (22.1 per cent) of postoperative peritonitis. This does not include cases in which operation was performed when peritonitis was already present, such as cases of gangrenous appendicitis or of ruptured ulcer. Resection for carcinoma was responsible for most of the postoperative deaths. There were 10 cases of peritonitis which developed after paracentesis for ascites and 126 cases (12.6 per cent) due to acute appendicitis, in some of which peritonitis developed after operation. One hundred cases (10 per cent) were due to tuberculosis and 27 (7.7 per cent) to infection from abortion. There were 45 cases (4.5 per cent) of peritonitis of primary or undetermined origin. Peritonitis occurred in 13 cases (1.3 per cent) of strangulated hernia, in 10 cases (1 per cent) of typhoid, in 6 cases (0.6 per cent) of septic sore throat, in 7 cases (0.7 per cent) of erysipelas, in 2 cases (0.2 per cent) of phlegmonous gastritis and in 2 cases (0.2 per cent) of bacterial endocarditis.

The incidence of peritonitis after operations is interesting, as is also the rather high incidence of tuberculosis of the peritoneum. The fatal cases of peritonitis resulting from perforation of a peptic ulcer numbered 48 (4.8 per cent). The ages of these patients ranged from 12 to 81 years. In 16 cases the perforated ulcer was in the stomach; 10 of these cases occurred in males and 6 in females, the ages averaging from 18 to 76 years. In 45 cases (4.5 per cent) no local or distant focus of infection could be demonstrated. One third of the patients in this group were under 1 year of age, but the ages of the remainder ranged

13. Pflaum, C. C.: A Postmortem Analysis as to Etiology in One Thousand Cases of Peritonitis, Am. J. Clin. Path. **5**:131 (March) 1935.

up to 70 years. Bacteriologic studies made in 20 of these cases showed streptococci in 16, staphylococci in 2 and pneumococci and diplococci in 1 case each.

The greatest incidence occurred in patients from 20 to 30 years of age. In the majority of cases the peritonitis had its origin in diseases of the gastro-intestinal tract. In adults in the third and fourth decade the primary lesion was usually found in the appendix or in the female genital organs. In late life peritonitis developed most frequently in cases of strangulated hernia, mesenteric thrombosis, malignant tumor and inflammation of the male genito-urinary tract.

TYPES OF PERITONITIS OF SPECIFIC ORIGIN

Four of the types of peritonitis of specific origin will be considered: bile peritonitis, pneumococcic peritonitis, tuberculous peritonitis and gonococcic peritonitis.

Bile and Liver Peritonitis.—Bile peritonitis may result from rupture of the gallbladder, with bile escaping freely into the peritoneal cavity. Here the bile is usually contaminated by the infection which causes the rupture, and the picture resembles that of spreading peritonitis.

Another type of bile peritonitis is that in which the bile seems to traverse the gallbladder without obvious signs of perforation. This type was first described by Clairmont and von Haberer [14] in 1910. Bile-stained fluid was found in the peritoneal cavity without visible perforation, and it was concluded that the bile ducts had been rendered permeable by some unusual pathologic process. However, this was not definitely established, as it is probable that perforation may have been overlooked. It seems, however, that such an escape of bile may occur in experiments in which the common duct is ligated and pancreatic juice is injected into the gallbladder. The gallbladder in animals then apparently becomes porous and permits bile to escape without any obvious perforation. Bundschuh,[15] according to Deaver,[16] has demonstrated that a similar process occurs in man when bile filters through the gallbladder as a result of obstruction in the bile ducts. However, all of these views seem to show that a lesion must exist in the gallbladder before the bile escapes, and the lesion is accompanied either by infection or by the digestive action of pancreatic juice. In such instances, the bile acts largely as a medium for conveying bacteria, much as in per-

14. Clairmont, P., and von Haberer, H.: Gallige Peritonitis ohne Perforation der Gallenwege, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **22**:154, 1910.

15. Bundschuh, E.: Der perforationslosen Gallenperitonitis, Arch. f. klin. Chir. **161**:549, 1930; quoted by Deaver.[16]

16. Deaver, J. Montgomery: Peritoneum, in Piersol, F. A.: The Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, 1934, pp. 743-774.

foration of any other viscus. The type of bile peritonitis, however, which may be considered as producing different symptoms is that in which uncontaminated bile escapes. This may follow a wound of the gallbladder or, more frequently, operations on the common duct or the gallbladder in which bile escapes.

In drainage of the common duct, which is a frequent procedure after the duct is opened for the removal of stones, bile usually escapes around the drainage tube, but adhesions quickly form and conduct it to the surface, though there may be some obstruction along the drainage tract which forces the bile into the peritoneal cavity. Instances in which the gallbladder is removed and the abdominal wall closed without drainage and bile escapes may be due to faulty ligation of the stump of the cystic duct, to a wound in some accessory ducts which were not observed at operation or to injury to the common duct. It is in such cases that true uncomplicated bile peritonitis occurs. This bile does not appear to have a very irritating effect at first, but if it escapes in large quantities or if the pressure is not relieved, the bile insinuates itself about the diaphragm, and death may occur. If the bile is mixed with pancreatic or gastric juice, as in perforation of the duodenum, the infection is much more violent. If the perforation permits the free escape of duodenal contents, death from shock may occur in a few hours.

In some interesting work on bile peritonitis by Moon and Morgan,[17] it was found that the intraperitoneal injection of sterile bile into animals produced a severe illness, frequently characterized by symptoms of shock. Death in coma resulted in twenty-four hours. The death seemed to be characteristic of shock. Moon and Morgan found that intravenous injections of sterile normal dog bile produced symptoms similar to those which followed injection into the peritoneal cavity. Their conclusions were:

> Intraperitoneal or intravenous injections of bile or of sodium glycocholate produce the shock syndrome characteristically in dogs. This is accompanied by hemoconcentration as in shock otherwise produced. Sublethal degrees of shock follow sublethal doses of the agents mentioned. These may recover or may result in pulmonary edema, pneumonia and subsequent death. The postmortem findings are the same as those following shock otherwise produced. These are: marked capillary and venous engorgement of the lungs, serosa, gastro-intestinal mucosa, liver and kidneys; edema of lungs, gastro-intestinal mucosa, and serous effusions; anemia of the splenic substance. The evidence indicates that bile or its salts cause acute injury to the walls of capillaries and venules. This results in atony and increased permeability, whereby a disparity develops between blood volume and volume-capacity of the vascular system. Such a disparity manifests itself in the shock syndrome.

17. Moon, Virgil H., and Morgan, David R.: Shock in Bile Peritonitis, Proc. Soc. Exper. Biol. & Med. **34**:743 (June) 1936.

The subject of liver peritonitis is largely of interest experimentally but may have some clinical bearing in cases in which the liver is traumatized and portions of injured liver tissue are in the free peritoneal cavity. First of all, the condition of the normal peritoneal cavity in the human being must be considered. According to Roberts, Johnson and Bruckner,[18] who made a study of the peritoneal cavity in 209 subjects, 80 per cent of the specimens from the peritoneal cavity contained different types of bacteria, and bacteria seemed to be found just as often in the absence of an inflammatory reaction as in its presence. They expressed the belief that the term "aseptic peritoneal cavity" is a misnomer. However, Trusler, Reeves and Martin [19] have shown experimentally that in removing peritoneal exudate accidental contamination is likely to occur. They have developed a technic which reduces the incidence of this contamination markedly. The contamination may be from various sources—from the margins of the skin in the wound, for instance. The greatest care should be taken to prevent this. Experimentally they use the cautery to incise the skin, heat the needle and take full precautions to prevent incidental contamination. The results of these experiments are interesting.

Andrews, Rewbridge and Hrdina [20] claimed that when sterile preparations of liver or bile salts are injected into the peritoneal cavity of a dog, death frequently occurs because of infection by the Welch bacillus, which is a normal inhabitant of the tissue of the dog. Trusler, Reeves and Martin [19] expressed the belief that these deaths are probably not due to infection by the Welch bacillus, which is often difficult to demonstrate but can be found by special staining and cultural methods. Numerous anaerobic gas-producing bacteria which might be confused with this bacillus and which do not produce an exotoxin in vitro are found normally in the liver and tissues of a dog. Many of these are saprophytic. In no instance were they able to isolate the Welch bacillus or any organism that produced an exotoxin in vitro. They found, however, that if the liver tissue was sterilized and injected into the peritoneal cavity soon after removal from the dog, there was slight if any toxic effect. When, however, the liver tissue was incubated for forty-

18. Roberts, K.; Johnson, W. W., and Bruckner, H. S.: The Aseptic Peritoneal Cavity—A Misnomer, Surg., Gynec. & Obst. **57**:752 (Dec.) 1933.

19. Trusler, Harold M.; Reeves, James R., and Martin, Hugh E.: Significance of Anaerobic Organisms in Peritonitis Due to Liver Autolysis, Arch. Surg. **30**:371 (March) 1935.

20. Andrews, E.; Rewbridge, A. G., and Hrdina, L.: Causations of Bacillus Welchii Infections in Dogs by the Injection of Sterile Liver Extracts or Bile Salts, Surg., Gynec. & Obst. **53**:176 (Aug.) 1931. Harkins, H. H.; Harmon, P. H.; Hudson, J., and Andrews, E.: Mechanism of Death in Bile Peritonitis, Proc. Soc. Exper. Biol. & Med. **32**:691 (Feb.) 1935.

eight or seventy-two hours and then sterilized in an autoclave and injected into the peritoneal cavity in the uncontaminated state, death resulted within a few hours from shock and peritonitis, and no bacteria could be recovered. This reaction was doubtless due to some toxic product that formed during the period of incubation, before the bacteria were killed. Neither the sterile liver nor sterile bile salts, according to Trusler and his co-workers, seemed to cause an infection of the peritoneal cavity by any bacteria.

In a further communication, Trusler and Martin [21] made some interesting observations. They found that when 70 Gm. of parenchymal elements of fresh liver was injected intraperitoneally they were essentially harmless. When as much as 50 Gm. of blood vessel, bile ducts and connective tissue of the liver was injected, the animal died. Animals given intraperitoneal injections of the epithelial cellular elements of the liver appear able to sterilize this material, while animals receiving the other portions of liver tissue died with bacterial growth in the peritoneal cavity.

These observations show the importance of removing the necrotic or devitalized liver tissue in cases of intra-abdominal trauma in which the liver is involved.

Pneumococcic Peritonitis.—Pneumococcic peritonitis is comparatively rare, but it appears to be a clinical entity. It was first described in 1865 by Bozzolo, when he reported a case occurring in Turin. Since then groups of cases have appeared in the literature from time to time. The disease appears more frequently in Germany and in France than in America. The infection may arise from one of four ways: from the blood stream in cases of disease of the respiratory tract, such as pharyngitis, bronchitis or pneumonia; by penetration from the diaphragm in cases of disease of the lung; by penetration from the wall of the bowel in cases of pneumococcic infection of the intestine, and through the uterus and fallopian tubes in cases of infection of the vagina. All of these routes have some advocates, but the two most probable sources of infection are from the blood stream in cases of infection of the lungs, trachea or pharynx and through the vagina. The last route was strongly advocated by McCartney and Fraser [22] in 1922. They cited an interesting group of cases in which pneumococcic peritonitis occurred in female infants and children. McCartney expressed the belief that pneumococcic peritonitis is frequently due to

21. Trusler, Harold M., and Martin, H. E.: The Cause of Death in Liver Peritonitis, Surgery **1**:243 (Feb.) 1937.

22. McCartney, J. E., and Fraser, J.: Pneumococcal Peritonitis, Brit. J. Surg. **9**:479 (April) 1922. McCartney, J. E.: Pathogenesis of Primary Pneumococcal Peritonitis, J. Path. & Bact. **26**:507 (Oct.) 1923.

uncleanliness and to contamination in the vagina, which is transmitted through the uterus and tubes. His observation that the disease occurs largely in persons in the lower social strata is not confirmed by the reports of most other authors. The acknowledged predominance in the female, however, is suggestive, and in almost every group of cases there are at least a few instances in which there is actual vaginal discharge or in which smears from the vagina show pneumococci of the type found in cases of peritonitis.

While pneumococcic peritonitis occasionally occurs in adults, the great majority of cases are found in children under 10 years of age, usually girls. The disease often follows the type of pharyngitis and coryza that occurs with a common cold, and it may also follow pneumonia. It occurs rather frequently, too, in children with ascites due to nephrosis, and the mortality in this group seems to be greater than in others. Cole [23] reported a group of 26 cases of pneumococcic peritonitis, in 10 of which there was ascites due to nephrosis. Five of the patients were male and 5 were female. In the remaining 16 cases, however, there were only 3 males.

Bass,[24] of Mount Sinai Hospital, New York, reported 19 cases, all of which were in females, but he does not include the cases of pneumococcic peritonitis in which there was also ascites due to nephrosis.

In a typical case, the patient, a young child, becomes extremely ill and complains of severe abdominal pain referred to the lower part of the abdomen and the umbilicus. There is high fever, a rapid pulse, vomiting and often diarrhea. The diarrhea occurs in 30 or more per cent of the patients and is an unusual finding in other types of peritonitis. There is often intense prostration, and death may occur within twenty-four hours after the onset of the disease. In other cases the pain diminishes, signs of intraperitoneal fluid appear and the patient gradually recovers after evidence of localization of the exudate in one part of the abdomen. The condition in these cases may be of long standing and may be mistaken for tuberculous peritonitis. Not infrequently pneumonia sets in as a complication after pneumonococcic peritonitis has developed. Other complications, such as endocarditis, otitis and nephritis, may occur.

Occasionally the greatest pain and tenderness may be in the right iliac fossa, in which case the differentiation from appendicitis may be difficult. Fever occurs early in the disease, often before there is tenderness or muscular spasm. The muscular rigidity is not marked, and in most instances Cole [23] described it as being of a doughy nature. Disten-

23. Cole, Warren H.: Pneumococcus Peritonitis, Surgery **1**:386 (March) 1937.

24. Bass, Murray H.: Pneumococcus Peritonitis, M. Clin. North America **19**:847 (Nov.) 1935.

tion usually does not occur until the third or fourth day of the disease. The tenderness, sometimes beginning in the lower right quadrant, is more likely to be diffuse. A feature that has been noted in this disease by many writers is the prominence of the umbilicus. If the early days of the acute stage can be weathered and the patient begins to improve, the exudate often localizes about the navel, and if the patient is not operated on, the pus may actually break through the navel.

A positive blood culture is obtainable in about half of the cases, but not until the second or third day of the disease. The leukocyte count is usually high, frequently as high as 40,000, though in rare instances it may be normal.

It is necessary to make a differential diagnosis between appendicitis and pneumococcic peritonitis. If the diagnosis cannot be reasonably determined otherwise, aspiration of the abdomen with a spinal puncture needle should be done and a drop or two of the peritoneal exudate should be withdrawn and examined as a smear. If numerous organisms are present with a predominance of colon bacilli, peritonitis of an appendical origin may be considered highly probable, but if only a single organism is present the peritonitis is probably not of appendical origin. Short-chain streptococci alone sometimes may be difficult to distinguish from pneumococci, but even so peritonitis due to these organisms will probably not have its origin in the appendix. If gram-positive diplococci or pneumococci are present, the diagnosis of pneumococcic peritonitis is confirmed.

The exudate at first is a thin, cloudy, yellowish free fluid with many flakes of fibrin. This accumulates in large quantities. After a few days it thickens and becomes a pure pus, usually retaining a greenish tinge but with many large masses of fibrin. Perforation at the umbilicus, which has been mentioned, may take place whether the pus is encapsulated or not. Occasionally there may be large abscesses in the pelvis.

The peculiar features about this type of peritonitis are its tendency to occur in female infants or children, the frequent accompaniment of diarrhea, the high leukocyte count which is usually present, the absence of intense muscular spasm and the tendency for the fluid to accumulate around the umbilicus.

The treatment seems to be medical, at least in the early stages. Operation in the first stage probably does more harm than good. Whatever may be the source of the infection, its original focus, unlike appendical peritonitis, cannot be removed, and there seems to be no point in draining a small area while the disease is progressing elsewhere. After the pus has localized, however, operation, consisting of a simple incision and the insertion of a small drain, is indicated. Not infrequently there may be several points of localization which must be drained.

General supportive treatment should be given, with rest to the gastrointestinal tract by refraining from enemas and depending for the supply of water and electrolytes and calories chiefly on the intravenous injection of dextrose in Ringer's solution.

Pneumococcus types 1 and 4 appear to be the organisms most frequently found in cases of pneumococcic peritonitis. Cole [23] reported that antipneumococcic serum was used in several instances with but little benefit, though in 2 cases it seemed to have a favorable effect. In 1 case the patient had nephrosis, and the improvement following the administration of antipneumococcus serum was striking.

Gonococcic Peritonitis.—Another specific form of peritonitis is that due to the gonococcus. This infection almost invariably follows gonococcic salpingitis and is a diffusion of the irritating effect from the gonococci that reach the tubes from infection in the vagina. The spread of gonococcic peritonitis beyond the pelvis is rare. Doubtless many of the cases that have been reported as following this course have been from a mixed infection.

The mucosa of the tubes becomes infected, then the submucosa and muscular coat are reached and, finally, the peritoneum will be infiltrated with the exudate. The irritation of the peritoneum causes adhesions, which limit the progress of the disease. It is a well known tendency of the gonococcus to excite fibrinous exudate, and this in itself prevents the extension of peritonitis. Thick creamy gonococcic pus escapes from the fimbriated ends of the tubes into the peritoneal cavity, and this excites fibrinous exudate, which often closes the tubes. The extensive subperitoneal edema and fibrinous exudate on the surface of the peritoneum are the outstanding pathologic features. Usually there is no general abdominal tenderness, but it is localized in the pelvis and around the uterus.

The history of a preceding vaginal discharge which has continued for some time with exacerbations of the pain in the pelvis, the protective exudate around the tubes and the limitation of the disease to the pelvis are the characteristics of the disease.

The treatment consists of rest and the application of heat. External heat applied to the abdomen and heat applied to the vagina after the very acute stages have passed seem to be helpful. In the early acute stages vaginal heat should be avoided, though applications of heat to the abdomen are indicated. Hypodermic injections of a nonspecific protein, such as milk, are often beneficial. The application of heat through the vagina by the Elliott method and the application of heat over the abdomen or by the endotherm method are helpful. A form of heat treatment by which the whole body except the head is subjected to a high temperature caused by electrical therapy seems to be beneficial in

many cases. It is well known that the gonococcus does not stand a high temperature, and heat seems to be peculiarly suitable for the treatment of this disease.

Patients with gonococcic peritonitis and salpingitis should not be operated on as a rule. Even after the disease has subsided, salpingitis may be cured with the applications of heat through the vagina and the general principles of rest. If a collection of pus appears in the cul-de-sac, it may be opened by vaginal puncture, but disturbing the fibrinous exudate in the cul-de-sac without definite localization of pus may make matters worse. Owing to the nature of the infecting organism, this type of peritonitis is radically different from the peritonitis caused by infection from the gastro-intestinal tract, as from the appendix.

Tuberculous Peritonitis.—Tuberculosis of the peritoneum may be found at any age, though most frequently before the twentieth year. In middle life or later, tuberculous peritonitis is usually a terminal stage of a process that has existed for many years. Tuberculous peritonitis may be divided into two forms: the primary form in which no other focus of the disease is present and the secondary form in which a focus can be demonstrated elsewhere.

The primary form is probably rare, because a small focus that might have furnished the original source of tuberculosis of the peritoneum may have healed.

In the secondary form the primary focus may be difficult to detect. The bacteria are borne by the blood stream, as not infrequently occurred when it was the practice to operate on cervical tuberculous lymph nodes.

Diffuse tuberculous peritonitis is probably caused by infection of the blood stream from some primary focus of tuberculosis elsewhere. Tuberculous peritonitis is, of course, different from the localized tuberculosis of the abdominal viscera, such as in the ileocecal region and the fallopian tubes, which are occasionally the site of a primary tuberculosis. In the ileocecal region tuberculosis of the bowel may assume a form in which there is great thickening and infiltration of the cecum and the terminal portion of the ileum with large tumor formation. In this type there is much plastic exudate, and the disease involves the entire wall of the bowel, though not infrequently the mucosa seems intact. The peritoneum over this region is secondarily affected, and usually the infection is localized.

Tuberculosis of the peritoneum is often found in delicate children, though it may occur in children who are apparently in good health.

When the disease does occasionally begin from the superficial parts of the ileocecal region or the fallopian tubes, the onset may be acute, with chills, high temperature, abdominal pain and slow distention, some-

what as in typhoid. In the majority of cases, however, tuberculosis of the peritoneum has a rather insidious beginning, and there will be discomfort, general weakness and indefinite abdominal pains; the abdomen will become distended, and sooner or later free fluid will be demonstrated. Occasionally localized symptoms develop. Loops of intestines may become adherent and enclose a collection of fluid closely resembling a cyst. Not infrequently there is diarrhea. In women irregular menstruation, amenorrhea or leukorrhea occurs as part of the symptoms of the disease. Even when the symptoms are mild, there is usually a rise of temperature in the afternoon.

The course of the disease is irregular. Much, of course, depends on the significance of the primary focus. Many patients recover completely.

In the miliary form the onset is usually acute and attended quickly by ascites. The peritoneum is covered with small grayish white tubercles that lie within the peritoneum, elevating it in small prominences. Sometimes they merge together and form a larger nodule very similar to metastasis from a malignant tumor. On the other hand, they may be so small as to be difficult to see, though they may be palpable with the finger.

Tuberculous peritonitis often originates in the peritoneum in the ileocecal region and the fallopian tubes. As the disease progresses, the tubercles usually become larger and project more markedly. The surrounding peritoneum will show an inflammatory reaction. The exudate is thin, clear and straw colored, quite different from that in the ordinary septic peritonitis and particularly different from that found in the later stages of pneumococcic peritonitis in which there is thick pus, usually with a greenish tinge. The abdomen is markedly distended, and the fluid can be easily demonstrated. The fluid when withdrawn may remain liquid or may coagulate, occasionally forming jelly-like masses.

The fibrinous form of tuberculous peritonitis may resemble the miliary form, but the exudate is more of a fibrinous nature. When the fluid is in the free state, it is usually too poor in fibrin, but if there is much tissue reaction, fibrin forms and adhesions occur. This may possibly be a sequel of the miliary form in which the exudate is more abundant, or the two processes may exist to some extent in the same case. When there is marked toxicity, the exudate remains fluid or semifluid because the toxic products prevent the formation of fibrin. When the fluid is absorbed, the dry type of tuberculous peritonitis results, though in some regions there may be encapsulated free exudate. The type in which fibrin occurs is that in which the fibrin content in the exudate is abundant. This may be present in the beginning of the

disease, or it is possible to have a gradual change from one form into the other. Usually fully developed connective tissue is not formed from this fibrin, though this may occur and adhesions of connective tissue show part of the healing process. As the healing progresses, however, the adhesions commonly loosen and are absorbed. The fibrinous activities may continue in the subperitoneal tissue with great thickening of the walls of the peritoneum. In such instances the tissue is so thickened that the gross appearance of tuberculosis will be lost, and the peritoneum will resemble parietal pleura in cases of advanced tuberculosis of the lung.

The caseous type results when there is marked thickening, and exudation and degeneration occur. The process is the same here as in tuberculosis elsewhere. The toxic material liquefies the tissue, and ulceration may result. When ulceration occurs, the exudate becomes granular and agglutinates the adjoining coils of the intestine, thus protecting the surrounding region against perforation. The spaces between the loops of intestine in such a type of tuberculous peritonitis may be filled with caseous contents, and histologic examination discloses the typical appearance of the tubercle. In the acute form there may be no tubercles easily demonstrated, but microscopic examination may show the tubercle bacilli. Giant cells are not necessarily indicative of tubercles. Not infrequently in chronic irritation of the peritoneum particles of fibrin are encapsulated and giant cells form around them.

The treatment of tuberculous peritonitis depends somewhat on the type of the disease. However, under all conditions the general treatment for tuberculosis should be instituted. Rest, with the administration of as much nutritious food as can be retained, fresh air, proper direction of the diet and the avoidance of chilling of the body are as essential in tuberculosis of the peritoneum as in tuberculosis elsewhere. Exposure to sunshine and heliotherapy are often helpful but should be given cautiously. Much harm may be done by excessive or improperly directed light treatment.

The treatment of the disease in the exudative stage, in which there is abundant ascitic fluid, has been the subject of much controversy and discussion in former years. There were strong advocates of various operative technics, many of which seemed to be successful in the early stages. They varied from an abdominal incision and exposure of the patient so that sunlight would fall into the abdomen for a short while to incision and drainage, manipulation of the intestines and dusting with various kinds of powder. Patients not infrequently recovered after any one of these treatments. It is now known, however, that all of these technics probably produced hyperemia of the intestines, and it was the hyperemia, whether it was caused by removal of ascitic fluid,

manipulation of the intestines or dusting with some powder, which benefited the disease.

If the disease appears to have originated from the peritoneum of the fallopian tubes and is more abundant in this region than elsewhere, possibly excision of the tubes may be justified, but as a rule in this type of superficial involvement of the peritoneum with tuberculosis any manipulation other than that intended to produce general hyperemia and a reduction of the exudate by drainage is unwise.

In the dry type of tuberculous peritonitis with numerous adhesions but little can be done in the way of surgical treatment. Manipulation in such cases not infrequently causes breaking down of the bowel and the formation of a fecal fistula, which adds to the misery of the patient and is difficult to heal. Such a patient should be treated medically in the same manner that a patient with tuberculosis elsewhere in the body would be treated.

CAUSE OF DEATH FROM PERITONITIS

Death from peritonitis is probably due to the absorption of toxins produced by the bacteria. This toxic absorption may be overwhelming within twenty-four hours, and death may occur from shock in which the splanchnic nerves are profoundly affected. The introduction of a considerable quantity of ice water into the peritoneal cavity in animals, according to Hertzler,[1] may produce death by shock. An overwhelming dose of toxic material in a subject with poor resistance may cause shock, and the sudden outpouring of large amounts of duodenal or gastric contents into the peritoneal cavity may prove fatal due to shock. If the patient survives a few days, the toxic material from the bacteria affects almost all of the vital organs. The heart is affected as well as the kidneys, the liver and the brain.

The chief point in the treatment of peritonitis is the prevention of the absorption of toxic material, which may begin soon after an operation or perforation and which depends on the amount of septic material present, the virulence of the sepsis and the resistance of the patient. The septic products are absorbed largely through the blood vessels. Some toxic material is taken up by the lymphatics to the lymph nodes, but a comparatively small amount goes directly through the lymphatic duct; consequently, the operation of draining the lymphatic duct in the neck is of no value in peritonitis, because this duct drains chiefly the lacteals.

TREATMENT OF PERITONITIS

The treatment of specific and rarer forms of peritonitis, such as pneumococcic, gonococcic, tuberculous and bile peritonitis, has been briefly discussed in the description of the disease. The most common

form of peritonitis is the septic form which has its source in the gastro-intestinal tract, and preventive treatment and therapy to be used after the disease has developed demand fuller consideration. As will be seen from the reference to the table by Pflaum,[13] in which he reports the results of necropsy in 1,000 cases of peritonitis, the most common cause of death was peritonitis developing after operation. This does not include cases in which peritonitis existed at the time of operation, such as instances of appendical peritonitis or of peritonitis due to rupture of a peptic ulcer. It is surprising that 22 per cent of all the deaths were due to peritonitis arising after operation.

I shall first consider local peritonitis. By local peritonitis is usually meant the type caused by aseptic irritation of the peritoneum, such as is found accompanying acute cholecystitis. This forms an exudate, and not infrequently the gallbladder becomes adherent to the surrounding tissue. The viability of the gallbladder is high, and in most cases the inflammation subsides and the bacteria do not penetrate the wall of the gallbladder. However, in some instances the gallbladder may become gangrenous and rupture. This converts an aseptic local peritonitis into a septic local peritonitis, which may extend, depending much on the resistance of the tissues and the nature of the infection.

Local peritonitis from the appendix is different because of the uncertain vascularity of the appendix and its proneness to rupture or become gangrenous and the fact, too, that its contents are usually far more virulent than the contents of the gallbladder. While, then, it frequently is wise to treat local peritonitis such as develops around the gallbladder expectantly because of the tendency of the inflammation in the gallbladder to resolve, local peritonitis around an inflamed appendix is another problem and should usually be treated by removing the focus of infection, the appendix.

The general principles of the treatment of spreading peritonitis may be stated as the removal of the focus of infection, if possible, the institution of drainage, the provision of rest to the gastro-intestinal tract and the administration of a sufficient amount of water, electrolytes and calories intravenously in order to give this rest. There are exceptions to some of these recommendations, such as in cases of general or spreading peritonitis in which the focus of infection cannot be definitely determined and in cases of so-called idiopathic or primary peritonitis, which may result from hematogenous infection by streptococci or possibly from small emboli carried in the blood stream that may produce minute permeable foci in the gastro-intestinal tract. In such instances drainage with continual pouring out of septic material into the peritoneal cavity from an irremovable focus will do little good. Drainage accompanied

by the elimination of the focus of infection, however, seems to be a safe principle whenever it can be adopted.

Much work has been done on the prevention of peritonitis after surgical operations on the gastro-intestinal tract. The portion of the gastro-intestinal tract involved is of great importance. In the stomach and upper part of the small intestine the bacterial content is low, and an open operation frequently can be done with comparative safety, provided the gastric juice contains a normal amount of acid. Lower in the small bowel and in the large bowel the content of the intestine is extremely septic, and in the large bowel, with its irregularity of contour, poor blood supply and slow healing, sepsis is peculiarly likely to occur when the bowel is opened. As a preliminary precaution in operations for cancer of the stomach, if the acid content of the gastric juice is absent or low, a 0.25 to 0.5 per cent solution of hydrochloric acid should be given abundantly for two or three days before the operation. This is a natural antiseptic in the gastric juice, and if there is a fungous growth or a necrotic lesion in the stomach, it diminishes the bacteria and makes safer any operation either on the stomach or on the upper part of the small intestine where bacterial growth is more abundant when hydrochloric acid is absent in the gastric juice. The natural resistance of the patient should also be improved by diet, transfusions of blood and the intravenous administration of water and electrolytes. Frequently the condition that calls for operation will prevent absorption of the food most desired.

In operations on the large intestine the so-called aseptic technic is usually unsatisfactory. Approximation cannot be accurately made, the amount of diaphragm turned in must be extensive and irregular and the basting stitches when pulled out not infrequently will be found to be contaminated. In union of the ileum to the transverse colon, preferably end to side, this aseptic technic is more effective because here it does not matter how much diaphragm is inverted and because the liquid contents of the small bowel make it improbable that constriction in this area will be sufficient to prevent the ileum from emptying. Elsewhere in operations in which the colon is solely involved it would seem better to reduce the virulence of the bacteria and give the tissues rest by complete cecostomy in which the ascending colon is brought onto the abdominal wall, a glass rod is placed through its mesentery, the cecum is opened and the entire current of fecal matter is delivered through the cecostomy opening. This not only gives rest to the remaining part of the colon and permits cleansing it with irrigations for two weeks before resection but allows an abundant diet to be given to improve the patient's general resistance.

In the matter of direct preparation for the prevention of peritonitis, numerous substances have been injected into the peritoneal cavity before operation, with the purpose of establishing relative local immunity. They have included various strengths of dextrose solution and other materials, but the two best known preparations have been amniotic fluid extract, which has been sponsored by Young, Johnson and Marks, and vaccine products with the colon bacillus as a base.

The preparation of amniotic extract was used by Johnson, his first report being made in 1927.[25] Young and Marks[26] reported a series of 49 clinical cases, many of them involving operations on the large intestine. The exact type of operation, however, is not given. In these 49 cases there were 3 deaths, 1 apparently being from pneumonia without peritonitis, and the other 2 from peritonitis.

Rankin and Bargen[27] developed a vaccine made from colon bacilli and streptococci. Some surgeons have injected various solutions of dextrose into the peritoneal cavity a few days before operation.

The purpose of administering these substances is not to effect a true vaccination in the sense of obtaining general constitutional immunity but to increase the local resistance of the peritoneum by bringing about a heavy influx of phagocytes, chiefly the polymorphonuclears. The value of these so-called vaccines has not been definitely determined, though apparently they have not justified the high hopes that were felt for them at one time. Thus, Rankin,[28] who once believed that the mortality rate from peritonitis subsequent to operations on the large bowel was materially reduced by the use of the vaccine which he and Bargen developed, recently stated that he had abandoned the use of the vaccine and secured equally good results without it.

Steinberg,[29] in reporting on the use of amniotic fluid experimentally, stated that it apparently had no beneficial effect in preventing peritonitis

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25. Johnson, H. L.: Observations on the Prevention of Postoperative Peritonitis and Abdominal Adhesions, Surg., Gynec. & Obst. **45**:612 (Nov.) 1927; An Exposition of the Preparation and Administration of Amniotic Fluid Concentrate, New England J. Med. **212**:557 (March 28) 1935.

26. Young, Edward L., Jr., and Marks, G. A.: Pre-Operative Preparation of the Peritoneum in Surgery of the Large Intestine, Surg., Gynec. & Obst. **59**:610 (Oct.) 1934.

27. Rankin, F. W., and Bargen, J. A.: Carcinoma of the Colon: Intraperitoneal Vaccination by Mixed Vaccine of Colon Bacilli and Streptococci, Arch. Surg. **19**:906 (Nov.) 1929. Rankin, F. W.: Vaccination Against Peritonitis in Surgery of the Colon: Further Report, ibid. **22**:98 (Jan.) 1931.

28. Rankin, F. W.: Resection of the Rectum and Rectosigmoid by Single or Graded Procedures, Tr. Am. S. A. **54**:155, 1936; Ann. Surg. **104**:628 (Oct.) 1936.

29. (*a*) Steinberg, B.: The Experimental Background and the Clinical Application of the Escherichia Coli and Gum Tragacanth Mixture (Coli-Bactragen) in Prevention of Peritonitis, Am. J. Clin. Path. **6**:253 (May) 1936. (*b*) Steinberg, B., and Goldblatt, H.: Protection of the Peritoneum Against Infection, Surg., Gynec. & Obst. **57**:15 (July) 1933.

in dogs. On the other hand, the "colibactragen" of Steinberg seems to be beneficial. Coller and Ransom [30] reported that in all of their patients in whom a one stage operation for excision of the rectum was performed and the peritoneum was protected by the colibactragen of Steinberg, the hyperleukocytosis it produced was worth while. They have used this intraperitoneal injection three hundred times with no apparent ill effect.

This preparation of Steinberg [29] has been vastly improved in the past two years. Formerly it was necessary to give it intraperitoneally at least forty-eight hours before the operative procedure, introducing it through a spinal needle or a small trocar. This was frequently followed by a rather severe reaction, and in several instances in which I used it it was necessary to postpone the operation until the patient recovered from the reaction. However, after five or six days it seemed to have a protective effect. The severity of the reaction was a distinct

TABLE 1.—*Results of Attempted Protection Against Peritonitis in Dogs*

Material Used	Dogs Used	Dogs Surviving	Dogs Surviving, Percentage
Tragacanth alone	15		
Typhoid bacteria in tragacanth	4		
Milk with tragacanth	4		
Amniotic fluid	4		
Aleuronat alone	4	1	25
Aleuronat in tragacanth	10	3	30

disadvantage. The recent preparation of Steinberg is much superior to the former one; the height of protection occurs within a few hours, and the colibactragen may be put in the peritoneal cavity during the operation. The patient is not adversely affected by the reaction. This colibactragen consists chiefly of killed colon bacilli suspended in salt solution and tragacanth U. S. P. By numerous and careful studies, Steinberg and his colleagues have found that this material will cause in the peritoneal cavity a vast outpouring of leukocytes, particularly of polymorphonuclears, which destroy the bacteria.

Steinberg now finds that if the colon bacilli, instead of being heat killed, are killed with formaldehyde, the period of heightened immunity is greatly shortened to about three hours, so that the colibactragen can be introduced at the time of operation.

His formula for the colibactragen as now made is as follows:

Tragacanth (ribbon)	1.5 per cent (1.5 Gm.)
Aleuronat	0.5 per cent (0.5 Gm.)
Escherichia coli (300)	2,400,000,000
Salt solution (0.85 per cent)	100 cc.

30. Coller, Frederick A., and Ransom, Henry K.: The One Stage Procedure of the Treatment of Carcinoma of the Rectum, Tr. Am. S. A. **54**:163, 1936; Ann. Surg. **104**:636 (Oct.) 1936.

Aleuronat is a diabetic flour and seems to stimulate the formation of the leukocytes in the bone marrow. The action of the tragacanth appears to be largely in retarding the absorption of the bactragen. Ordinarily when a solution of soluble toxins and dead bacteria is placed in the peritoneal cavity it is quickly absorbed and the influence is ephemeral, but the tragacanth prevents this quick absorption and spreads the influence of the colibactragen over a period of at least several days. That the colibactragen acts in this manner and not constitutionally is shown by Steinberg [29a] in a patient in whom the fat of the abdomen was so great that the colibactragen was accidentally injected into the deep layers of the abdominal wall instead of into the peritoneal cavity. No reaction followed. However, when this mistake was realized, a peritoneal injection was made and the usual reaction occurred.

Strains of colon bacilli have been found by Steinberg [29] to be more effective in bringing out the leukocytes than any other bacteria. This preparation is not specific for colon bacilli but affects streptococci found in cases of peritonitis which originate in the gastro-intestinal tract. This is shown by the engulfing of the various bacteria by the phagocytes. The experiments apparently do not clarify the role that the humoral antibodies may play, but they do not show any evidence that they play an important part.

When this colibactragen is introduced, the phagocytosis attacks the bacteria irrespective of the species of bacteria and is usually complete in from four to eight hours. The presence of the large number of polymorphonuclears in the peritoneal exudate, the free bacteria and the observation of the leukocytes that contain ingested bacteria in the protected dogs contrasted with the small amount of leukocytes in the control dogs seem to indicate the manner in which this colibactragen works. When it is used, the bacteria appear to remain almost entirely in the peritoneal cavity, where they are consumed by the phagocytes, but without it they escape from the peritoneal cavity rather rapidly. In dogs with experimental peritonitis that are protected by this colibactragen the leukocytes are apparently diminished in number in the first hour, but in the second and third hours they are markedly increased, whereas in the nonprotected animals there is a consistently low number of leukocytes.

It must be emphasized that this protection is not specific against a single organism but is effective against a mixed bacterial infection and that phagocytosis is accomplished before the production of the toxic soluble substances by the bacteria and that these soluble toxic substances are responsible for death from peritonitis. The essential purpose of this colibactragen is to allow the slow passage of the leukocyte-stimu-

lating substance from the peritoneum to attract leukocytes into the peritoneal cavity. However, after the toxins have developed they seem to inhibit the phagocytosis by the leukocytes; so the colibactragen is not effective in the treatment of established peritonitis.

The use of this colibactragen is doubtless helpful in preventing peritonitis. Of course it must be employed along with other measures, which have already been mentioned—the improvement of the patient's resistance, the transfusion of blood, the treatment of dehydration, the administration of a nutritive diet, and a proper operative technic. No vaccine can be expected to be efficient against a leaking suture.

In the treatment of established peritonitis the Fowler posture is helpful, not because the peritoneum in the pelvis absorbs less readily than that at the diaphragm but because the posture tends to gather the exudate in one localized region of the peritoneum and because, too, the pumping action of the diaphragm may accelerate absorption in the upper portion of the abdomen.

Drainage is one of the important therapeutic agents in the treatment of peritonitis, but it should not be used indiscriminately. If the perforation of a peptic ulcer can be closed within ten hours after the perforation and the peritoneal fluid withdrawn with a suction apparatus, drainage is usually unnecessary. In idiopathic peritonitis from hematogenous infection, drainage probably does but little good. When, however, the peritonitis is from some local focus, such as the appendix, drainage is valuable. The fluid that accumulates around an acutely inflamed appendix which has not ruptured is often protective and does not need drainage. It consists chiefly of leukocytes and lymph. When pus has accumulated and there is spreading peritonitis, drainage is indicated. The drainage should not be too abundant. A medium sized soft rubber tube with several perforations and one or two cigaret drains, consisting of iodoform gauze in a rubber dam tube, are usually all that is necessary.

Drainage of infection that begins from a definite focus, as in cases of appendicitis, serves to remove the exudate that is in this region and so lessens the amount of soluble toxin that might be absorbed through the peritoneal cavity. It must be recalled that mechanical removal of the exudate is not the sole function of drainage. An important function is the biologic effect that the drain has as a foreign body exciting an outpouring of lymph from the surrounding tissues in nature's effort to extrude it. Thus, even though the drainage tract may be soon walled off by exudate, the presence of the drain as a foreign body stimulating an outpouring of lymph toward it is beneficial and retards absorption of toxic products near the drain.

If it can be determined that the peritonitis is caused solely or chiefly by a hemolytic streptococcus, treatment with sulfanilamide should benefit. Large quantities of fluid should be given, not by mouth or by rectum but by the intravenous administration of 5 per cent dextrose in Ringer's solution, so providing physiologic rest for the gastrointestinal tract. Five per cent dextrose in distilled water is indicated if it seems that there is an undue accumulation of salt. Stronger solutions of dextrose, such as 10 per cent, may be administered for a short time, but they tend to irritate the vein, and the 5 per cent solution is isotonic.

On general principles, the source of the infection should be eliminated if possible. Thus, in perforation by a peptic ulcer or a typhoid ulcer, it is essential to close the perforation. This should be done as simply as possible. In cases of peptic ulcer there seems to be no need to cauterize the ulcer or to do any extensive operation. If the ulcer is in the duodenum the perforation may be closed by a series of mattress sutures placed transversely along the margin of the ulcer and tied gently, so they will not pull out, and this is reenforced by one or two other rows of sutures. The last sutures bring over peritoneal covered fat or omentum.

The treatment of the distention and the adynamic ileus that accompany peritonitis is important. The introduction into the stomach of a Jutte or Levine tube, which was first advocated by Matas,[31] who also first advised the continuous intravenous injection of a 5 per cent solution of dextrose, is indicated. Recently this has been developed and elaborated by Wangensteen [32] and others and is now in general use.

As a precautionary measure in almost every operation on the abdomen which is prolonged or which involves the stomach or intestine, a Jutte tube should be inserted until the patient can take food. This may be connected with a suction apparatus, as developed by Wangensteen.

The administration of morphine is helpful in cases of peritonitis. Attention was called to this by Plant and Miller [33] and by Gruber and

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31. Matas, Rudolph: Continued Intravenous "Drip," with Remarks on the Value of Continued Gastric Drainage and Irrigation by Nasal Intubation with Gastroduodenal Tube (Jutte) in Surgical Practice, Ann. Surg. **79**:643 (May) 1924.

32. Wangensteen, O. H.: Therapeutic Considerations in Management of Acute Intestinal Obstruction: Technic of Enterostomy and Further Account of Decompression by Employment of Suction Siphonage by Nasal Catheter, Arch. Surg. **26**:933 (June) 1933.

33. Plant, O. H., and Miller, G. H.: Effects of Morphine and Some Other Opium Alkaloids on the Muscular Activity of the Alimentary Canal, J. Pharmacol. & Exper. Therap. **27**:361 (June) 1926.

Robinson.[34] Thomas G. Orr,[35] of Kansas City, Ochsner [36] and others have demonstrated experimentally the tonic effect of morphine on the intestines. Orr [35] found that "morphine and related opium derivatives when given hypodermically stimulate the tone, rhythmic contraction, and in some degree peristaltic waves of the small intestine for a period of at least six hours" and advised maintaining the tone and contractions of the bowel by the use of morphine hypodermically in the treatment of acute peritonitis, intestinal obstruction and paralytic ileus. It should be given in sufficient doses to cause a continuous narcosis.

Ochsner,[36] in a description of the postoperative care following abdominal operations, emphasized these measures and advocated also the application of heat to the abdominal wall preferably by means of a heat tent, which acts beneficially, not by increasing the congestion of the intestinal tract but by increasing the somatic circulation and decreasing the splanchnic blood supply. There seems to be a reciprocal blood supply between the splanchnic and the somatic area, and whenever there is a dilatation of the vessels in the splanchnic area there is contraction of the vessels in the somatic area. This dilatation in the somatic area produced by heat decreases the congestion in the abdominal viscera, diminishes the secretion of the intestine and lessens the dilatation of the bowel.

As acute appendicitis is a frequent and important source of general peritonitis, it may be well to discuss it more specifically. The general principles of the removal of the septic focus, of supplying water, electrolytes and dextrose solution and of giving the bowel a rest should be followed. The same principle which demands the closure of a perforation from an ulcer as soon as the diagnosis is made should also apply to appendicitis. In the upper part of the abdomen it has been well demonstrated that the mortality rate from ruptured peptic ulcer increases with the delay of operation, and in the lower intestinal tract where the bacteria are far more abundant this rule should apply even more strongly. It would seem evident, therefore, that an appendix which has perforated and which has admitted bacteria to the peritoneal cavity and continues to admit them should be removed as soon as possible. If, however, this is to be done through a long abdominal incision with extensive sponging and rough handling of the tissues, probably

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34. Gruber, C. M., and Robinson, P. I.: The Intestinal Activity in Unanesthetized Dogs as Influenced by Morphine and by Papaverine, J. Pharmacol. & Exper. Therap. **37**:101 (Sept.) 1929.

35. Orr, Thomas G.: The Action of Morphine on the Small Intestine and Its Clinical Application in the Treatment of Peritonitis and Intestinal Obstruction, Ann. Surg. **98**:835 (Nov.) 1933.

36. Ochsner, Alton: Postoperative Treatment Based on Physiologic Principles, South. Surgeon **4**:197 (June) 1935.

more harm than good will result, and it would be best to trust to nature to wall off and limit the peritonitis until an abscess has formed. It must be recalled that in the early stages of peritonitis the eventual result is established, and, while the patient may not die immediately, if the peritonitis is poorly handled fatal errors will have been committed from which there can be no recourse.

The general principles of treating acute appendicitis should be those that apply in other perforations of the intestinal tract. They may be stated briefly as follows:

1. Operate at any stage as soon as the diagnosis is made.

2. Make a McBurney incision, through which the appendix may be approached and drainage, if necessary, established.

3. Always remove the appendix.

4. Use suction to remove pus or exudate; do not place gauze within the peritoneal cavity, and on no condition sponge away the pus or the exudate.

5. Treat the stump of the appendix simply, by merely tying it and disinfecting it. Do not bury the stump.

6. Give the bowel rest by refraining from proctoclysis and enemas at all times and by supplying the water, electrolytes and calories by intravenous continuous injection of 5 per cent dextrose in Ranger's solution.

These principles are self-evident. Unless they are followed through collectively, however, they should not be attempted, for they are dependent on each other. For instance, there is no point in attempting to remove an appendix from fibrinous exudate if at the same time the bowel is to be packed off with gauze and the pus sponged away with gauze. Each time the pus is sponged away, bacteria are forced by the sponge into the tissues. It is practically the same as if the septic material were actually injected into the tissues. If a suction apparatus is not available, at any rate the pus or liquid exudate should not be sponged; it might be drawn off with a syringe. The necessity of giving the bowel a rest is also obvious. It is a truth laid down by Hilton in "Rest and Pain" that is one of the classic foundations of treatment, and if the inflamed bowel is to be given exercise in absorption or motion by the introduction of water through proctoclysis or nutrition or purgatives through the mouth, this well established principle is being violated. While it is necessary to supply water, electrolytes and, to some extent, calories, this can be readily done intravenously with the proper precautions by means of the continuous direct flow, without the drip apparatus. The dangers from thrombosis are increased by too concentrated a solution and by the use of the drip apparatus which may permit aspiration

of air if the patient strains and obstructs the flow and then suddenly the flow is increased. This can be prevented and made much simpler by merely regulating the flow with a thumbscrew clamp and observing the level of the solution in a graduated container.

Robertson,[37] of the pathologic department of the Mayo Clinic, said: "For a long time I have been, in season and out of season, inveighing against the custom of burying the stump of the amputated appendix. It strikes me as wholly illogical and, worse than that, a dangerous procedure. The well known ostrich with his head in the sand hasn't very much on this custom." Robertson has found that up to the twenty-first day there is always a pocket of pus in an inverted stump of an appendix. The logic of covering a raw surface does not obtain in this instance, because by inverting the stump of the appendix one is burying necrotic material within a cavity the nutrition of which is impaired

TABLE 2.—*Appendectomies Done at St. Elizabeth's Hospital from Jan. 1, 1931, to April 1, 1937*

	Cases, Number	Deaths, Number	Deaths, Percentage
Acute appendicitis	449	3	0.67
Acute appendicitis with abscess formation and localized peritonitis	60	1	1.67
Acute appendicitis with spreading generalized peritonitis	29	1	3.45
Subacute or chronic appendicitis	188	0	0
Carcinoma of appendix	1	0	0
Total	727	5	0.69

by a purse-string suture and dangling it in the most septic part of the intestinal tract.

Since Jan. 1, 1931, the surgical staff at St. Elizabeth's Hospital has adopted the principles that have been described. No single one of these is new or original. Several of them, such as the use of the McBurney incision, operating whenever the diagnosis is made and the simple treatment of the stump of the appendix, have been used for many years, but the combination of all of these principles, including suction and giving rest to the bowel by the intravenous injection of dextrose in Ringer's solution, has so far as I know not been previously practiced.

The surgical staff of this hospital, consisting of Dr. John S. Horsley, Jr., Dr. Guy W. Horsley[38] and me, operates in every case of acute appendicitis as soon as the diagnosis is made, at whatever stage the disease may be. The total number of cases in which appendectomy was performed from Jan. 1, 1931, to April 1, 1937, is 727. This does

37. Robertson, H. E.: Personal communication to the author.

38. Horsley, Guy W.: Improved Treatment of Appendicitis with Results in Five Hundred and Two Consecutive Cases at St. Elizabeth's Hospital, Virginia M. Monthly **62**:598 (Jan.) 1936.

not include cases in which the appendix was removed incidentally during another operation but only cases in which the operation was done solely or chiefly for appendicitis. The results are shown in table 2.

Of the 3 deaths from acute appendicitis, 1 resulted from a pulmonary embolus in a man aged 59 who had a gangrenous appendix. He recovered and was about to leave the hospital, when he was suddenly stricken with a pulmonary embolus and died in a few minutes. Another death was that of a very obese man who suffered from chronic alcoholism with a bad liver and kidneys. The appendix was removed. Paralytic ileus and uremia developed, and the patient died the sixth postoperative day. Necropsy showed no peritonitis. The third death was that of a patient who had acute appendicitis and also an abscess of the tube on the left side which involved the ileum. The appendix was removed. The abscess and part of the ileum had to be resected. Five days after operation the patient died from intestinal obstruction and localized peritonitis on the left side.

Abcess and localized peritonitis were the cause of death of a man 72 years of age who had a retrocecal appendical abscess. During convalescence he had pulmonary edema and cardiac weakness, from which he died four days after the operation.

The fifth death was in a neglected case of generalized peritonitis in which there was gangrenous bowel which had to be resected in the presence of infection.

In none of the fatal cases was there uncomplicated appendical spreading peritonitis.

COMEDO CARCINOMA OF THE BREAST

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In many of the articles and special treatises dealing with carcinoma of the breast no mention is made of the variety called comedo. In some instances such a tumor may have been described under another caption, but the description is not clear enough to justify one in believing that the author had in mind the type of lesion discussed here. There is undoubtedly confusion in the minds of some as to the significance of the term comedo. The point may be illustrated by quoting a statement accredited to one of the leading pathologists:[1]

> Next we turn to the histological and anatomical varieties of duct carcinoma. Nearly all carcinomas of the breast arise from ducts. Duct carcinoma gives rise to a type of tumor which runs along the ducts and reproduces ducts, and for a long time shows a relation to and a respect for ducts. The types are the localized and the diffuse. In a localized form of duct carcinoma we usually find a small breast, a little fat near the nipple; but there is apt to be marked cicatrization. Cancer begins in the ducts near the nipple, and produces a localized cancerous mass in a small and contracted breast. This is sometimes supported by dilated ducts 1 mm. or so. Yellowish or black-like acne pustules in the skin may form and on that account, this type is sometimes called comedo carcinoma (a good term). The comedo appearance may be seen in all forms of duct carcinoma.

As a matter of fact, the term comedo is applied to such a tumor because when it is cut plugs of tumor cells may be expressed from the ducts, giving an appearance much like that produced when the plug or comedo is expressed from an ordinary blackhead. The term has nothing to do with any changes that may be noted in the skin during the clinical course of this variety of carcinoma.

As far as can be ascertained from a careful search of the literature, Bloodgood was the first to give the name comedo to this type of growth. The following quotation is taken from an article published by him in the *American Journal of Cancer* in 1934:[2]

> In 1893, forty-one years ago, I assisted Dr. Halsted in exploring a benign tumor of the breast. The patient was sixty-seven years of age and had observed

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From the Surgical Clinic and the Laboratory of Surgical Pathology of the Johns Hopkins Hospital.

1. Ewing, James: Lectures on Tumor Pathology, New York, Cornell University Medical School, 1934, p. 139.

2. Bloodgood, J. C.: Comedo Carcinoma (or Comedo-Adenoma) of the Female Breast, Am. J. Cancer **22**:842, 1934.

a small tumor for about eleven months. It was our custom then to cut into the tumor and decide on its pathological nature from the naked-eye appearance of the tissue. This tumor was not encapsulated and not cystic, but distinctly circumscribed and buried in a senile breast. The moment we cut into and pressed on it, there exuded from its surface many grayish-white, granular cylinders, which I called at that time comedos. From the gross appearance the tumor was diagnosed as malignant, and the radical operation was performed. The nodes were not involved, the breast was senile, and there was no gross or microscopic evidence of chronic cystic mastitis. The patient lived nineteen years after operation, dying at the age of eighty-six.

Since then I have been recording such cases and have divided them into two groups—pure comedo-adenocarcinoma and comedo-adenocarcinoma with areas of fully developed cancer of the breast. Examples of the latter group, in which areas of pure comedo are present in an otherwise fully developed cancer of the breast, are the more frequent, and for this reason the operator must always bear in mind the possibility of cancer when comedos are present in a tumor. Hence, if the tumor is too large to exclude the presence of malignant areas by frozen section, a radical mastectomy should be done.

In an inaugural dissertation entitled "Carcinoma Intracanaliculare Proliferans Mammae," Selling [3] described the histologic changes in a tumor of the breast which had been surgically removed. Unfortunately the clinical history could not be obtained. The specimen measured 7 cm. in length, 4 cm. in width and 3 cm. in thickness. The growth was of a papillary nature, which was distinctly demonstrated when water was allowed to flow over the tumor. The tissue spaces contained many nests of tumor cells, and the blood vessels were apparently involved. The histologic characteristics of this tumor are quite different from those of the duct carcinoma described later, and the probabilities are that in the case described by Selling the growth originated in the acini and the ducts were secondarily involved. The title of the dissertation would seem to accentuate the proliferating potentialities of the growth which led to extensive invasion of the lymphatic spaces.

Dietrich and Frangenheim [4] stated:

It has not been determined whether the carcinoma with intracanalicular extension originates in the epithelium of the ducts (Jacobaeus). Early cases of this type are not known, and in advanced stages it is not possible to decide the relationship between the epithelium of the ducts and the carcinoma. Comparison with carcinomas of other organs does not permit one to conclude that there is a definite relationship between the duct epithelium and the carcinoma, although it apparently has been demonstrated conclusively in cases of Paget's disease.

The character of the cells of carcinoma growing in the ducts is the same as that of the cells of carcinoma solidum, but there is frequently a tendency to flattening

3. Selling, T.: Carcinoma Intracanaliculare Proliferans Mammae, Inaug. Dissert., Würzburg, P. Scheiner, 1898.

4. Dietrich, A., and Frangenheim, P.: Die Erkrankungen der Brustdrüse, in von Bruns, P.: Neue deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1926, vol. 35, p. 171.

and reduction in height, so that the cells resemble those of flat epithelium. Intracanalicular glandular carcinoma has been described (Ribbert).[5]

According to Cheatle and Cutler:[6]

The primary epithelial neoplasia in a duct carcinoma may arise by one of two methods of origin I and II. In both types the ampulla is a favourite site of origin. The larger ducts are also more favourite sites than the smaller ones. In this respect they resemble the benign papillomata. The ampulla is a dilated portion of a duct and stagnation of its contents is more liable to occur than in the large branches. The action of any form of irritation would be more marked in its effects when in a stagnant medium. Stagnation of contents would favour prolonged and undisturbed action of any irritant they might harbour.

I. The usual type consists in the formation of papillomatous irregularly branching stalks which are covered by atypical epithelium arranged in three or more layers. There are also small growths of sessile epithelial neoplasia, containing no connective tissue elements and arising from other parts of the duct wall. The structures of the growths may remain chiefly papillomatous and grow to large sizes by expanding the duct walls. In later stages of the tumour, all signs of duct walls disappear and the tumour is growing in outside tissues. Before such an extension of the chief growth has occurred, epithelial cells can be definitely seen invading the duct wall and spreading in surrounding tissues. These tumours are round, small, hard, solid and possess defined margins. Some specimens may show a much greater amount than others of sessile epithelial neoplasia compared to the papillomatous parts. In all instances there is a great tendency for the spreading cells in the chief mass of the tumour to line any connective tissue elements with which they come in contact. These cells remain columnar, upon which cells of all shapes are superimposed. In the early stages the papillomatous parts branch extensively before growing large, the branches coalesce at their tips and anastomose with neighbouring branches, and thus form alveoli lined by epithlium. The epithelium lining these alveoli multiply and cause them to be filled by cells of a variety of shapes and sizes. The tumours retain their round outlines and their properties of being movable beneath the skin without causing it to pucker for a long time before they become fixed to surrounding structures which include the skin. If left alone they ulcerate and fungate. Hæmorrhages are common in and from these tumours. Hæmorrhage may distend the peripheral branches of the ducts and blood may also be spontaneously discharged from the nipple.

II. [In the second type, one specimen], the tumour is seen in the dilated ampulla of a duct from the wall of which it arises by only one stalk. The tumour consists of ducts and acini. Parts of the tumour are undergoing cystiphorous desquamative epithelial hyperplasia. In other parts the epithelial growth has become so chaotic as to suggest that carcinoma has begun in this part of the tumour. Below the chief dilatation, two branches of the same duct are dilated by a multiradicular type of papilloma, the epithelial cells of which are everywhere limited by normal boundaries. There were no axillary glands affected in this case. There was no discharge of blood from the nipple. This specimen demonstrates the following points: (1) From the epithelium of a duct a tumour may arise containing all the elements

5. Ribbert, P., cited by Dietrich and Frangenheim.[4]

6. Cheatle, Lenthal G., and Cutler, Max: Tumours of the Breast, Philadelphia, J. B. Lippincott Company, 1931, p. 180.

of a normal breast, although they may be irregular in shape and arrangement. (2) The tumour has only one stalk. (3) The epithelial contents of the tumour may undergo cystiphorous desquamative changes similar to those that can be observed in otherwise normal breasts. . . . (4) This new breast formation may undergo carcinomatous changes and form a distinct type of duct carcinoma. At this point it is interesting to recall the fact that in benign, multiradicular papillomata, formation of ducts and acini can often be discovered.

This description applies to papillary carcinoma of the ducts rather than to the type of duct carcinoma described in this paper.

The duct carcinoma about to be described, we believe, represents a distinct type which frequently can be recognized clinically. In discussing duct carcinoma it must be remembered that in the development of the ducts there are two distinct phases of differentiation, and in the development of the acini, still another phase. The relation of adenocarcinoma to the terminal part of the tubules and acini is generally recognized. The origin of the carcinoma described by Paget from the germinal epithelium of the nipple and that of the primary ducts seems to be well established. The clinical and pathologic pictures of carcinoma arising from the epithelium of the branching mammary ducts between the nipple, the terminal portion of the ducts and the acini, however, have remained ill defined.

CLINICAL DESCRIPTION

Comedo carcinoma usually presents two rather characteristic pictures. Before discussing these, a few case histories will be given which will illustrate the clinical picture of the diffuse form.

CASE 1.—A. B., a Negress aged 63, had had two children. The menopause occurred at the age of 52. Seven years before admission to the hospital she discovered a small lump in the breast somewhat removed from the nipple and about the size of a pigeon's egg. She experienced pain from time to time and rubbed the lump with camphor liniment. After five and one-half years the tumor became as large as a hen's egg. Hot applications were then used. Two months before the patient's entrance to the hospital a yellowish discharge from the nipple was noticed. The skin covering the breast took on a pigskin appearance.

When the patient was examined, the right breast was found to be as large as a grapefruit and somewhat lobulated, but a single tumor could not be palpated. The overlying skin in areas appeared thinned, and small nodules could be palpated in it. A distinct pigskin appearance was noted (fig. 1). The breast was not fixed to the chest. No enlarged nodes were palpable in the right axilla. The enlarged breast was lobulated, and apparently a tumor which had an elastic feel occupied the anterior half. Because of these findings, a diagnosis of intracanalicular myxoma was made in spite of the lymphedema. A radical operation was performed on Feb. 23, 1934. When the tumor was incised, the cut surface had the appearance of a two by four which had been sawed across (fig. 2). Many epithelial plugs could be expressed from the cut surface. Suppurative phlebitis of the cephalic vein developed, and the patient died on March 10.

Fig. 1.—Typical appearance of a diffuse comedo carcinoma of the breast in a Negress 63 years of age. The tumor had been noted for seven years. The elevations seen in the skin are caused by the comedos in the ducts. The tumor resembled somewhat clinically an intracanalicular myxoma in being lobulated and imparting an elastic feel on palpation.

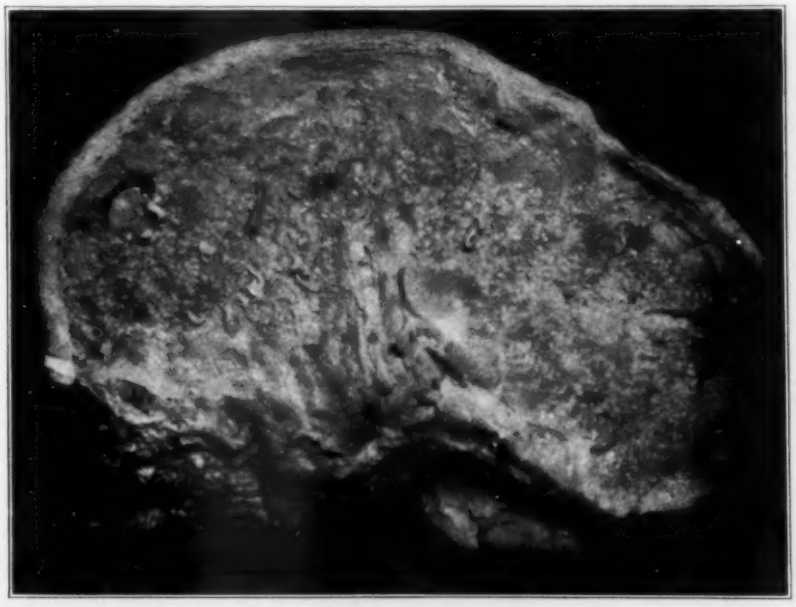

Fig. 2.—Cross-section of the breast shown in figure 1. The surface of the tumor resembles in appearance that of a two by four which has been sawed across. The comedos may be seen projecting from the surface of the tumor.

As has been stated, this diffuse comedo carcinoma presented some of the clinical features peculiar to intracanalicular myxoma.

CASE 2.—M. F., a white woman aged 34, noticed a lump in her breast eight months after childbirth. This breast had not produced milk. When examined, the patient stated that the tumor had been noted for four and one-half years. She had been pregnant a year before this examination was made. Four months before the examination pain developed in the breast. The breast then became red, and a discharge from the nipple was noted. The nipple became retracted, and the tumor increased rapidly in size. The patient's mother and her mother's mother both died of carcinoma of the breast. Both breasts were large, but the left was nearly twice the size of the right. The tumor was the size of a grapefruit, and was firm, lobulated and adherent in places to the skin. There were no palpable axillary nodes. A radical operation was performed on March 4, 1917. According to the operative note, no enlarged nodes were found. The pectoral muscles were not invaded. The patient was well and free from recurrences in 1936, nearly twenty years after the operation. Many dilated spaces were found on gross examination, and from these were discharged a yellowish fluid which resembled condensed milk. Histologically the tumor was a comedo carcinoma.

CASE 3.—L. S., a white woman aged 53, had had three children. The menopause occurred at the age of 42. One month before the present examination she felt a burning sensation in her left breast. She touched the area and found a tumor. She did not believe that the growth had increased much in size. On examination a mass about 7 cm. in diameter and without definite margins was found to the outside of the left nipple. The overlying skin was slightly dimpled. There were no palpable lymph nodes in the axilla. The complete operation for cancer was done on Nov. 14, 1932, following a biopsy. Plugs of solid material could be expressed from dilated ducts in the gross specimen. The microscopic diagnosis was comedo carcinoma. Examination of the lymph nodes for cancer gave negative results. The patient was seen on Dec. 5, 1935, at which time the roentgenograms of the spine and lungs did not show any evidence of metastases. A recent inquiry concerning the patient's present condition has not been answered.

CASE 4.—B., a white woman aged 48, had had seven children, whom she nursed. Since nursing her last child, three and one-half years before the present examination, she had noted a hardness of the right breast with crusting of the nipple, apparently due to a chronic discharge. On examination a hard mass which involved the entire upper half of the breast was palpated and some dimpling of the overlying skin was noted. A few drops of serosanguineous discharge was expressed from the right nipple. No enlarged lymph nodes could be palpated in either axilla. A radical operation was performed on Aug. 31, 1927. The gross specimen had the typical appearance of a comedo carcinoma. Plugs were expressed from the ducts. The diagnosis was confirmed by microscopic examination. Metastases were found in the midaxillary nodes but there were none in the nodes at the apex or base of the axilla. The patient died of metastases five years after operation.

The four cases have been reported to give the clinical picture of the diffuse comedo carcinoma. It is a slowly growing tumor which involves the greater part of the affected breast, and an isolated tumor cannot be palpated in the enlargement. Despite the size of the growth there are frequently no palpable lymph nodes. Small elevations in the skin may

be found, which are caused by the protrusion of the epithelial plugs within the ducts, and not infrequently a discharge from the nipple is noted.

In the localized form the tumor is small, measuring from 1 to 3 cm. in diameter. It is usually situated at the margin of the areola just beneath the skin and is freely movable. The axillary nodes, as a rule, are not involved, and not infrequently a yellowish or watery discharge from the nipple is noted. The affected breast is slightly larger than the uninvolved breast. The tumor differs from the intracystic papilloma and the blue dome cyst in that it is relatively harder and more irregular. A hard irregular tumor in the location just described and associated with atrophy of the overlying fat and a yellowish or milky discharge suggests a comedo carcinoma.

In the case described in the following report a tumor appeared in each breast.

CASE 5.—O. N., an unmarried woman aged 44, for five years noticed a swelling of the left breast, which was diagnosed as chronic cystic mastitis. The tumor grew rapidly, but no pain and no discharge from the nipple was noticed. On examination a hard mass was palpated just beneath the left areola. The mass measured about 2 cm. in diameter and was just beneath the nipple. Several large hard lymph nodes were palpated in the left axilla. A radical operation was performed on June 27, 1933. On gross examination the tumor was white and firm and the ducts contained plugs of carcinoma cells. The microscopic diagnosis was comedo carcinoma. In October 1933 a small tumor appeared in the opposite breast and in April 1934 the right breast was amputated. The patient was well in September 1937.

Bloodgood[7] in 1917, in a chapter on lesions of the female breast published in Binnie's "Regional Surgery," made the following statement:

> At the exploratory incision this [tumor] has such a distinct gross appearance that one should never fail to recognize it. Now I know that in the early tumor the typical comedo may be absent. In the past two years I have restudied all the cases of pure comedo and also those cases in which the comedo tumor was mixed with fully developed cancer. There is but one conclusion, and that is that pathologists can learn to recognize the pure comedo tumor in all its histological pictures by repeatedly studying the actual sections in those instances in which the tumor has been removed, the breast saved and the patients followed. The pure comedo takes its place among the borderline tumors of the breast which are of growing importance. It must be recognized in frozen and permanent sections if progress is to be made in diagnosis and treatment.

There is nothing unusual about the age incidence of comedo carcinoma, and in general it corresponds to the age incidence of other forms of carcinoma of the breast. One third of the patients observed by us were under the age of 45. In about 25 per cent the tumor was of over

7. Bloodgood, J. C.: Lesions of the Female Breast, in Binnie, J. F.: Regional Surgery, Philadelphia, P. Blakiston's Sons & Co., 1917, p. 611.

two years' duration, and in six it had been noted for five years or more. The location of the comedo carcinoma suggests an origin in the larger ducts. It often develops near the nipple at the margin of the areola, in many cases just above and to the outside of the nipple (fig. 3). Symptoms referable to the nipple are common. A watery, milky or yellowish discharge is noted not infrequently. Retraction or fixation of the nipple occurs often, and occasionally the patient complains of burning and itching of the nipple, a symptom more common in Paget's disease. In one case the nipple was destroyed as a result of ulceration. In a few cases a serosanguineous discharge from the nipple was noted.

The tumor is usually located near the skin, and atrophy of the overlying fat and dimpling of the skin occur. Redness of the skin is

Fig. 3.—Fungating comedo carcinoma of the breast of over two years' duration in a woman 55 years of age. (From Bloodgood, J. C.: Am. J. Cancer **22**:842 [Dec.] 1934.)

sometimes noted. The tumor remains movable. Even when the growth is larger than a large grapefruit and involves almost the entire breast, there will be no fixation to the wall of the chest. Several tumors may be found in the same breast. In three instances similar tumors were found in both breasts.

RESULTS OF TREATMENT

Of all the forms of carcinoma of the breast, comedo carcinoma offers the most favorable prognosis. At the time the data for this report were secured there were 85 per cent of five year cures in the group of cases observed by us. The majority of the patients living more than five years after operation have remained well for ten years

or more. Three patients have remained well more than twenty years, and a fourth patient has remained well for thirty-six years. The duct carcinoma composed of transitional epithelium—related to Paget's disease of the nipple—does not afford as favorable a prognosis. A five year cure was found in but 46 per cent of the cases of this type. Comedo carcinoma associated with scirrhous carcinoma was arrested for five years in but 25 per cent of the cases.

Forty of the forty-seven patients with comedo carcinoma could be traced sufficiently well to be included in this summary. No report could be obtained on four, and three have not been followed long enough (less than three years) to justify any conclusions as to the results. There are thirty-five patients on whom five year results can be based. Of these thirty-five, one died of metastases after five years, and the others died of metastases after four, three and two years, respectively. The remainder were well after five years—85 per cent five year cures. Of these, however, one died after six years, a cancer of the opposite breast having developed.

Fifteen of the twenty-three patients with duct carcinoma composed of transitional epithelium were traced. Two of these were well after four years. Of the remaining thirteen who could be followed, seven had died of metastases, and six were well over five years.

There were thirty-nine patients with combined comedo and scirrhous carcinoma. Of these, twelve were inadequately traced, leaving twenty-seven on which to base the five year results. Of these twenty-seven, nineteen are known to be dead of metastases. The remaining eight were well over five years, one, for thirteen years and another for twelve years—27 per cent of five year cures.

There were eight cases of comedo carcinoma in which the initial treatment consisted of local excision. In six of these the growth recurred locally—in four within one year, in one after eighteen months and in another after four years. In these cases radical operation was performed later. In three, metastases to the axillary nodes were found at the second operation. Local excision was done in two of three additional cases, and simple removal of the breast was done in the other. One of the patients, the wife of a physician, has remained well for eleven years, no other operative intervention having been necessary. A second patient is now well, showing no evidence of recurrence after three and one-half years. The third patient was treated with irradiation followed by amputation of the breast without axillary dissection. This operation was performed in May 1934, and the last report, made at the time of writing, stated that the patient was dying of metastases to the bone and to the skin over the wall of the chest.

TABLE 1.—*Data on Forty-Seven Cases of Comedo Carcinoma*

Case No.	Age, Yr.	Duration of Growth	Clinical Findings	Operation	Result
1	53	4 mo.	Pain in lateral portion of breast; discharge from nipple; tumor 6 cm. in diameter	7/22/37: Excision 8/11/37: C.C.*	Well in 1937
2	44	7 yr.	Hard and freely movable tumor 6 cm. in diameter	3/19/34: Excision	Well in Sept. 1937
3	35	3 mo.	Tumor of left breast near nipple; two similar lumps; comedos in gross specimen; discharge from nipple; tumor 0.5 cm. in diameter	July 1936: Biopsy; excision Oct. 1936: C.C. for recurrence	Well in Sept. 1937
4 (Case 1 of text)	63	7 yr.	Fungating tumor the size of a grapefruit	2/23/34: C.C.	Died 3/10/34 postoperatively
5	46	1 yr.	Tumor 1.5 cm. in diameter near a cyst	1935: C.C.	Well in July 1937
6 (Case 5 of text)	44	5 yr.	Tumor 2 cm. in diameter near nipple	6/27/33: C.C. 4/..34: C.C. of other breast	Well in Sept. 1937
7	29	3 mo.	Tumor 1 cm. in diameter near nipple	10/15/34: Excision 9/21/36: C.C. for recurrence	Well in Sept. 1937
8 (Case 3 of text)	53	1 mo.	Tumor 3 cm. in diameter	11/14/32: C.C.	Well 12/5/35; lost from observation in 1937
9	37	1½ mo.	Tumor 6 cm. in diameter near nipple; no discharge	8/13/32: C.C.	
10	38	9 mo.	Tumor 9 cm. in diameter near nipple; discharge	1/8/31: Excision 1936: C.C. for recurrence	Well in Sept. 1937
11	45	Routine finding	Tumor 2 cm. in diameter; comedos in gross specimen	5/21/27: C.C.	Well in Sept. 1937
12	32	2½ mo.	Tumor 2 cm. in diameter near nipple	12/ 5/28: C.C.	Died from other causes 8 yr. after operation
13 (Case 4 of text)	48	3½ yr.	Tumor involving one half of breast; sanguineous discharge from nipple	8/31/27: C.C.	Dead in 1932, 5 yr. after operation, of metastases
14	53	1 yr.	Tumor 3 cm. in diameter; freely movable; atrophy of fat	6/17/26: Excision	Well in Sept. 1937
15	56	2 mo.	Tumor 2.5 cm. in diameter near nipple; discharge	9/16/24: C.C.	Well in 1930
16	67	1 mo.	Tumor near nipple	6/ 6/24: C.C.	Died in 1930, 6 yr. after operation, from other causes
17	40	2 wk.	Tumor 2 cm. in diameter in right breast, just behind and above nipple	Dec. 1923: Excision Dec. 1924: C.C. for recurrence	Well in 1937, 14 yr. after first operation
18	39	3 mo.	Tumor 3 cm. in diameter near nipple; affected breast largest in midzone, with overlying red skin; no discharge; growth circumscribed but not encapsulated near skin; atrophy of fat	10/13/23: C.C.	Well in 1937, 14 yr. after operation
19	45	3 yr.	Tumor 8 cm. in diameter and 3 cm. from nipple; patient kept under observation for 1 yr.	12/ 5/22: C.C.	Died 4/26/37 from other causes
20	42	1 day	Tumor 2 cm. in diameter	7/13/22: C.C.	Well 4/13/37, 15 yr. after operation
21	45	10 mo.	Tumor 6 cm. in diameter; discharge from nipple	5/21/20: C.C.	Well in 1930, 10 yr. after operation
22	49	2 yr.	Tumor beneath nipple; nipple retracted; dimpling and itching; mass in axilla for 3 mo.	4/ 6/20: C.C.	Lost from observation
23	39	1½ yr.	Tumor the size of a grapefruit; discharge from nipple	1918: Excision 1919: C.C. for recurrence	
24 (Case 2 in text)	34	1 yr.	Tumor 4 cm. in diameter	3/22/17: C.C.	Well in 1937, 20 yr. after operation

* In this table and in tables 2 and 3, C.C. indicates complete operation for carcinoma.

TABLE 1.—*Data on Forty-Seven Cases of Comedo Carcinoma—Continued*

Case No.	Age, Yr.	Duration of Growth	Clinical Findings	Operation	Result
25	45	5 mo.	Tumor 3 cm. in diameter	10/12/16: C.C.	Died in 1919 of metastases
26	45	2 yr.	Tumor 2 cm. in diameter	9/18/16: C.C. of right breast 9/28/16: C.C. of left breast	Well in 1930, 14 yr. after operations
27	67	2 yr.	Tumor involving entire breast; burning, itching and ulceration 2 cm. from nipple; comedos in gross specimen; creamy discharge	6/—/16: C.C.	Died in June 1929, 13 yr. after operation, from other causes
28	52	5 yr.	Tumor in right breast; pain	6/—/16: C.C.	Well in 1932, 16 yr. after operation
29	55	6 yr.	Tumor 1.5 cm. in diameter near nipple	5/13/16: C.C.	Died 6/22/22 from cancer
30	41	5 yr.	Tumor near nipple	2/15/15: C.C.	Died in 1930, 15 yr. after operation, from other causes
31	38	2 yr.	Sanguineous discharge from nipple; tumor 2 cm. in diameter near nipple	3/ 5/14: C.C. of right breast 11/ 1/16: C.C. of left breast	Well in 1937, 23 yr. after first operation
32	55	1 yr.	Tumor involving whole breast; painful swelling; discharge from nipple	8/ 3/11: C.C.	Died in 1915 from cancer
33	45	3½ mo.	Tumor 5 cm. in diameter upper hemisphere of breast	5/11/10: C.C.	Died in 1912 of metastases to lungs
34	52	6 mo.	Tumor; discharge	2/22/09: C.C.	Well in 1922, 12 yr. after operation
35	60	Routine finding	Tumor the size of a grapefruit; discharge	.....	Died postoperatively
36	57	6 mo.	Tumor; discharge	5/29/06: C.C.	Well in 1913, 7 yr. after operation
37	43	1 mo.	Tumor 2 cm. in diameter near nipple; comedos in gross specimen	2/25/04: C.C.	Well in 1926, 20 yr. after operation
38	45	.....	.....	1904: C.C.	Well in 1933
39	43	1½ mo.	Tumor 2.5 cm. in diameter in outer upper quadrant of breast; no discharge from nipple; comedos in gross specimen	6/17/03: C.C.	Well 5/28/15
40	47	1 mo.	Tumor 3 cm. in diameter near nipple; retraction; discharge; creamy plugs	6/—/01: C.C.	Well in 1905, 4 yr. after operation, metastases to opposite axilla
41	48	1 yr.	Tumor 3 cm. in diameter above and lateral to areola, near skin; atrophy of fat; retraction of nipple; comedos in gross specimen	1/30/01: C.C.	Well in 1937, 36 yr. after operation
42	52	2 yr.	Bilateral tumor	1899: C.C.	Died in 1914, 15 yr. after operation, from other causes
43	42	1½ yr.	Tumor 5 cm. in diameter beneath nipple, hard; comedos in gross specimen	10/31/98: C.C.	Well in 1919, 21 yr. after operation
44	47	9 mo.	Tumor 2.5 cm. in diameter above nipple; skin red	10/29/98: C.C.	Well in 1919, 21 yr. after operation
45	61	6 mo.	Area of induration in upper outer quadrant of breast; comedos in gross specimen	1896: C.C.	Died in 1903, 7 yr. after operation, from pneumonia
46	42	3 mo.	Tumor 3 cm. in diameter in lower inner quadrant of breast	7/17/95: C.C.	Died 6 yr. after operation from cancer of opposite breast
47	65	17 mo.	Tumor 4 cm. in diameter in outer upper quadrant of breast; movable; comedos in gross specimen	7/ 8/93: C.C.	Died in 1912, 19 yr. after operation, of pneumonia

Bloodgood,[2] in a note to the article published in the *American Journal of Cancer,* stated:

> No new cases are added and all the evidence is that the pure comedo-adenoma does not give rise to metastases, and can be cured by excision of the local tumor only. When the tumor is of fungous nature or is too large for local excision, irradiation should be tried first.

The figures which we have presented would seem to show that eventually local operation has been followed by recurrence, but they also indicate that when a radical operation is performed a year or more after local excision because of recurrence a cure has resulted in spite of axillary metastases. Because of the difficulties encountered in determining the malignant potentialities of the duct tumor designated as comedo-adenoma, it would seem best to do a primary radical operation in all tumors of this type.

HISTOLOGIC DESCRIPTION

Comedo carcinoma arises from small oval cells with dense nuclei and scanty cytoplasm. These resemble the basal cells of the epidermis. There are numerous intermediate cell forms with increasing amounts of cytoplasm showing a differentiation into duct epithelium with an irregular secretory border. These cells form a thick lining or wall in the ducts. The larger secretory epithelium surrounds the central lumen of the duct, which contains secretory débris; the smaller basal cells rest on a basement membrane, which sharply demarcates the duct epithelium from the periductal fibrous tissue (fig. 4). The nuclei of the tumor cells are small and dense and in general show no conspicuously malignant features. All of the duct channels throughout one or more quadrants of the breast may show this characteristic hyperplasia of the lining epithelium. The tumor cells not only line preexisting ducts but form new secretory channels, so that small secondary openings appear in the cross-sections of the lining epithelium of the larger ducts. The tumor grows slowly and metastasizes late, if at all, to axillary lymph nodes. In cases in which metastases occur the epithelium in the lymph nodes shows the characteristic thick-walled ducts lined by secretory epithelium with numerous transitions toward basal cells. This characteristic histologic appearance of the metastases (fig. 6) indicates clearly that the tumor cells are capable of forming new ducts and are not simply invading preexisting ducts.

In the typical comedo carcinoma the tumor cells are confined by a basement membrane and form epithelial channels with solid or thick walls; invasion of fat or fibrous tissue is inconspicuous or absent. The

TABLE 2.—*Data on Twenty-Three Cases of Duct Carcinoma Histologically Resembling the Lesion of the Nipple Described by Paget*

Case No.	Age, Yr.	Duration of Growth	Clinical Findings	Operation	Result
1	39	9 mo.	Tumor 4 cm. in diameter	1/—/34: C.C.	Died in Oct. 1935 of metastases to lungs and pleura
2	43	4 mo.	Tumor; discharge from nipple; no enlarged nodes	8/ 1/33: C.C.	Well 10/3/37
3	56	4 days	.....	3/ 9/33: Excision of mass	Well 8/30/37
4	51	2 yr.	Scaly left nipple	7/ 1/31: C.C.	
5	40	.....	Tumor 6 by 8 by 9 cm. in upper outer quadrant of breast; solid	12/—/32: Biopsy 3/—/33: C.C.	Died of pulmonary metastases
6	44	1 mo.	Tumor 4 cm. in diameter; discharge from right nipple	8/ 4/32: C.C.	Well 8/31/37
7	37	1 wk.	Tumor 4 cm. in diameter	6/ 4/32: C.C.	Died of metastases
8	30	1 yr.	.....	9/17/31: C.C	
9	41	2 mo.	Indefinite mass, bleeding from nipple; no pain	11/—/31: Excision	Well in Dec. 1935
10	51	.....	.....	9/—/26: C.C. 9/—/28: Excision of lump and scar	Died 2/12/29
11	49	2 yr.	Tumor 1.5 cm. in diameter; pain; discharge	4/26/28. C.C.	Well in Jan. 1936
12	46	15 mo.	Tumor in right breast; pain	3/25/27: C.C. 1928: Amputation of left breast	Died in 1929 of metastases
13	35	3 yr.	Tumor 4 cm. in diameter in right breast; discharge	6/18/26: C.C.	Well in 1933
14	61	6 mo.	Tumor 3 cm. in diameter in right breast	12/ 9/25: C.C.	Well in 1926
15	64	6 mo.	Tumor 2.5 cm. in diameter in right breast; midzone near nipple	12/ 9/25: C.C	Well in 1931
16	58	7 wk.	Tumor of left breast; tenderness	6/ 5/25: C.C.	Died 4/13/28
17	39	5 yr.	Tumor 4 cm. in diameter in left breast; pain	8/15/24: C.C.	Well in 1931
18	25	1 mo.	Tumor 3 cm. in diameter in right breast; pain; comedos in gross specimen	12/ 8/21: C.C.	
19	34	3 days	Tumor 3 cm. in diameter in upper outer quadrant of breast toward midline	7/ 3/18: Excision 8/24/19: C.C.	Died in Feb. 1920 of multiple metastases
20	35	4 yr.	Tumor the size of a grapefruit; pain; discharge from nipple	3/ 3/17: C.C.	Well in 1926
21	40	1 yr.	Tumor	10/ 9/12: C.C. for recurrence	Died 1 yr. after operation, of metastases
22	41	9 mo.	Tumor 4 cm. in diameter in upper outer quadrant of breast near nipple; comedos in gross specimen	5/11/29: C.C.	
23	40	5 wk.	Tumor 0.5 cm. in diameter in upper inner quadrant of breast	6/10/07: C.C.	

TABLE 3.—*Data on Thirty-Nine Cases of Combined Comedo and Scirrhous Carcinoma*

Case No.	Age, Yr.	Duration of Growth	Clinical Findings	Operation	Result
1	55	1 yr.	Tumor 2 cm. in diameter in inner quadrant of breast; freely movable; no discharge	1/30/36: Excision 2/26/36: C.C.	Well in Sept. 1937
2	42	5 yr.	Tumor 5 by 4 by 2 cm. below nipple of left breast; attached to skin; no discharge; dilatation of veins	12/14/32: C.C.	Well 9/17/37
3	23	3 mo.?	Tumor 6 cm. in diameter; rapid growth	6/ 5/34: Excision	Well to 1936
4	54	2 mo.	Tumor 2 cm. in diameter medial to nipple; no discharge	5/ 1/34: Amputation only; preoperative irradiation, 1,800 roentgens	Died in Sept. 1937 of metastases to bone and skin
5	40	1 wk.	Tumor 2 by 3 cm. in upper inner quadrant of right breast; no discharge	4/30/32: C.C.	Well 10/1/37
6	65	6 wk.	Tumor 2.5 cm. in diameter in upper quadrant of right breast; dimpling; no discharge	1/29/32: C.C.	Well 9/17/37
7	63	6 wk.	Tumor 8 cm. in diameter in outer upper quadrant of left breast; hard, nodular and attached to skin	11/20/30: C.C.	
8	52	7 wk.	Lump in left breast; hard and firm	10/ 4/32: C.C.	Died in May 1933 of metastases to liver
9	25	3 wk.	Tumor; pain	6/10/30: C.C.	
10	54	3 wk.	Tumor; pain	3/ 3/30: Biopsy 3/29/30: C.C.	Well in Aug. 1936
12*	55	1 yr.	Tumor 6 cm. in diameter; intermittent swelling	3/16/26: C.C.	Died in June 1929 of metastases to lungs
13	47	6 wk.	Lump in nipple zone the size of a silver dollar; lump in axilla	10/15/26: C.C.	Died 3/4/29
14	45	6 mo.	Tumor 2 cm. in diameter in right breast; tumor 1.5 cm. in diameter in right breast	8/ 1/25: C.C.	Died in 1930
15	50	5 mo.	Tumor involving entire breast; redness and pigskin appearance of skin; retraction of nipple; irritation	2/17/25: C.C.	Died in 1926 of carcinosis
16	41	3½ mo.	Lump in breast with retraction of nipple; lump in axillary gland for 1 wk.	11/29/24: C.C.	Died in June 1925
17	52	4 yr. 2½ yr.	Nipple retracted; crust and mass beneath nipple	10/20/24: C.C.	Died in Feb. 1929 of pulmonary metastases
18	65	3 yr.	Tumor involving entire left breast; mass beneath nipple	10/10/23: C.C.	Died in 1925 of metastases to liver
19	32	6 mo.	Tumor 1.5 cm. in diameter in left breast	9/29/23: C.C.	Died in 1925 of metastases to lung
20	38	3 yr. (axilla) 3 wk. (breast)	.....	.....	Died in 1932 of metastases
21	51	.....	Tumor 7 cm. in diameter beneath nipple; comedos in gross specimen	2/27/23: C.C.	
22	32	3 wk.	Tumor 4 cm. in diameter in left breast	1/—/23: C.C.	Died in 1923 of metastases to lungs
23	41	12 yr. (pain) 6 mo. (tumor)	Tumor 2.5 cm. in diameter in upper outer quadrant of breast; atrophied over tumor	12/27/22: C.C.; postoperative irradiation	Died 4/29/36 of metastases to bone

TABLE 3.—*Data on Thirty-Nine Cases of Combined Comedo and Scirrhous Carcinoma—Continued*

Case No.	Age, Yr.	Duration of Growth	Clinical Findings	Operation	Result
24	24	1 mo.	Tumor 4 cm. in diameter in upper outer quadrant of breast; tumor 0.5 cm. in diameter below large mass	5/—/21: Excision 6/19/21: C.C.	Died in 1922 of metastases
25	49	14 yr. (lump) 10 yr. (tumor)	Upper outer quadrant of breast lumpy and sensitive; tumors 3 cm. in diameter near right and left nipples; no discharge; multiple lumps in both breasts	6/16/21: C.C.	Well in March 1935
26	39	3 yr.	Tumor near nipple; irritation	6/11/20: C.C.	Died 2/19/21 of metastases to skin
27	50	6 mo.	Tumor 3 cm. in diameter in left breast; pain; discharge from nipple	12/ 6/19: C.C. for recurrence	Died in 1920
28	35	1 yr.	Tumor 3 cm. in diameter in upper outer quadrant of breast	4/ 8/19: C.C.	
29	56	2 wk.	Tumor 3 cm. in diameter in outer quadrant below nipple; comedos in gross specimen; no discharge	10/ 6/17: C.C	Well 5/6/30
30	58	3 mo.	.....	4/18/17: C.C.	Died in 1921
31	44	6 mo.	Several tumors	7/20/16: C.C.	Well in 1919
32	..	.....	Tumor of left breast	5/16/15: C.C.	
33	37	1 mo.	Tumor 3 cm. in diameter	8/27/24: C.C.	Lost from observation
34	44	20 mo.	Tumor above and inside of nipple; no discharge; recurrence in upper outer quadrant of breast	2/14/14: Amputation only	Well in 1930
35	34	10 mo.	Tumor 6 cm. in diameter in upper outer quadrant of breast	9/18/13: C.C.	Lost from observation in 1937
36	45	3¼ mo.	Tumor 5 cm. in diameter in upper hemisphere of breast; atrophy of fat	7/11/10: C.C.	Died 10/2/11 of metastases to lung
37	47	5 mo. 3 mo.	Tumor above nipple Recurrent tumor in outer upper quadrant of breast; no discharge	5/11/05: C.C.	
38	47	2 yr.	Tumor 2.5 cm. in diameter	10/22/97: C.C.	Lost from observation in Jan. 1899
39	45	3 yr.	Tumor 8 cm. in diameter in upper inner quadrant of breast	3/21/94: C.C. 4/ 5/95: Resection of clavicle	Well in 1906, 12 yr. after first operation
40	47	7 mo.	Tumor in inner zone of left breast	10/23/14: C.C.	Dead 4/22/18 of metastases to spinal column

* Case 11 was deleted by the authors.

transition between basal cells and secretory epithelium occurs gradually with the persistence of numerous basal cell forms. The carcinoma described by Bloodgood as a "pure comedo" has a highly favorable prognosis, but it must be distinguished microscopically from duct cancer related to Paget's carcinoma and from adenocarcinoma with invasion of the ducts in which comedo-like areas are combined with areas of typical scirrhous carcinoma.

In duct carcinoma showing a histologic relation to Paget's cancer, the tumor cells approach squamous epithelium in type. The tumor cells have abundant cytoplasm and large dense or vesicular nuclei with numerous mitoses. Multinucleated giant tumor cells are common. Areas of central necrosis are seen within duct channels lined by such highly malignant epithelium (fig. 7). The tumor invades the large ducts, and ulceration of the nipple may occur, giving the classic clinical picture of Paget's carcinoma. The growth of the tumor is rapid, and

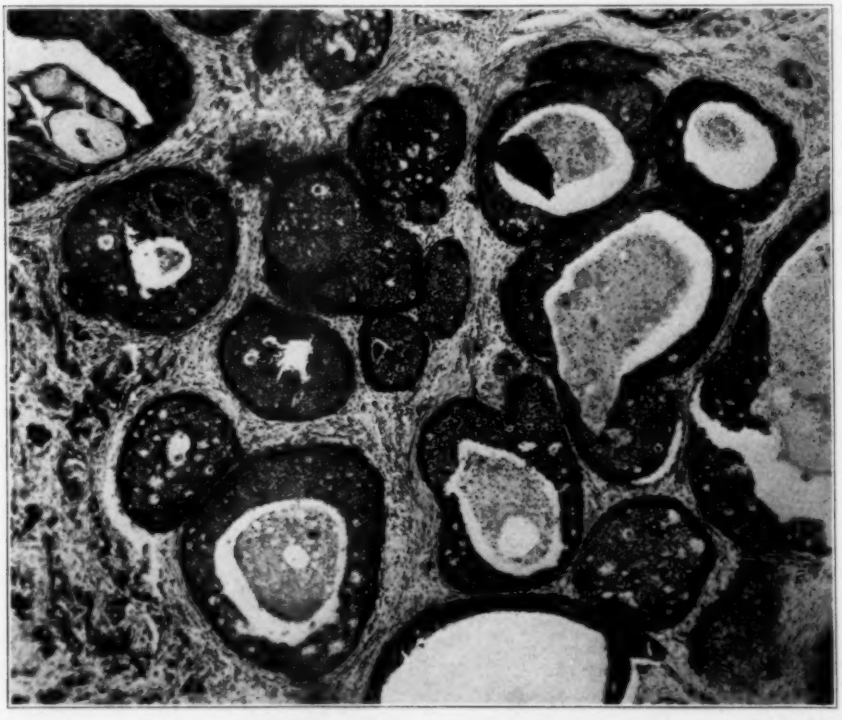

Fig. 4.—Photomicrograph of a typical comedo carcinoma showing ducts filled with epithelial plugs. Small new ducts are being formed in the epithelial plugs.

the prognosis is poor. This type of duct cancer is more closely allied in its behavior to Paget's cancer of the nipple than to comedo carcinoma.

In typical scirrhous carcinoma (infiltrating adenocarcinoma) areas of invasion resembling comedo carcinoma may be found occasionally in the smaller ducts. This tumor should not be confused microscopically with true comedo cancer. In carcinoma arising in the smaller ducts and terminal tubules there will be found under the microscope areas resembling comedo carcinoma. But invasion of fat and fibrous tissue by

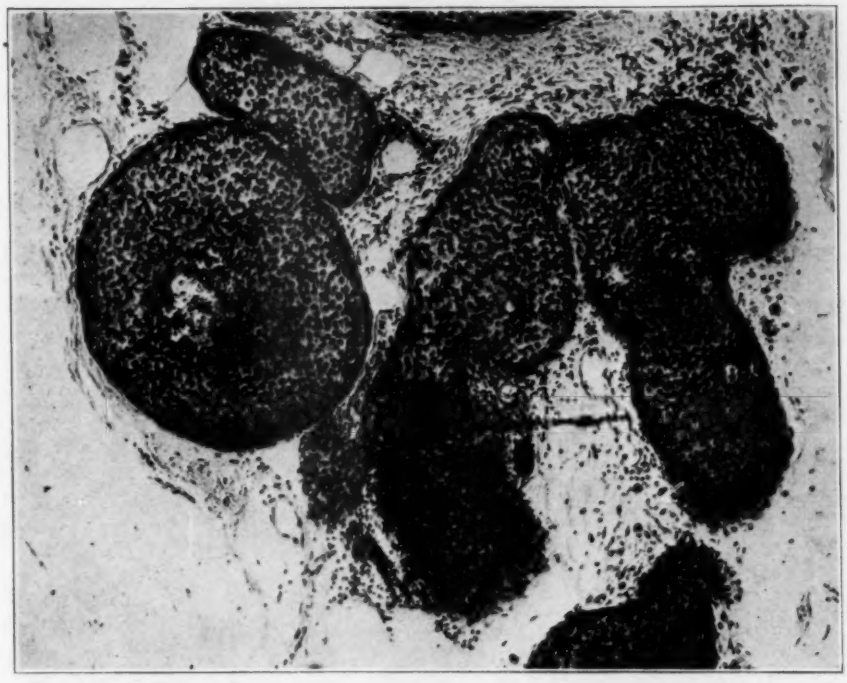

Fig. 5.—Photomicrograph of a comedo carcinoma showing the small basal cells from which the tumor develops.

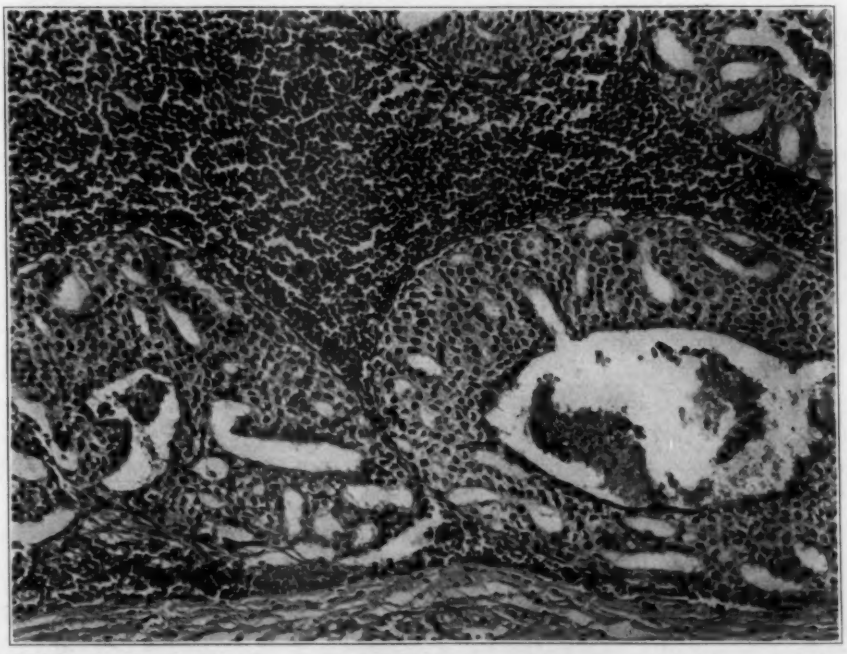

Fig. 6.—Section from an axillary lymph node showing metastases from comedo carcinoma of the breast primarily treated by excision. The brushlike border of secreting epithelium can be seen surrounding the lumen. The histologic picture indicates that the tumor cells are capable of forming new ducts.

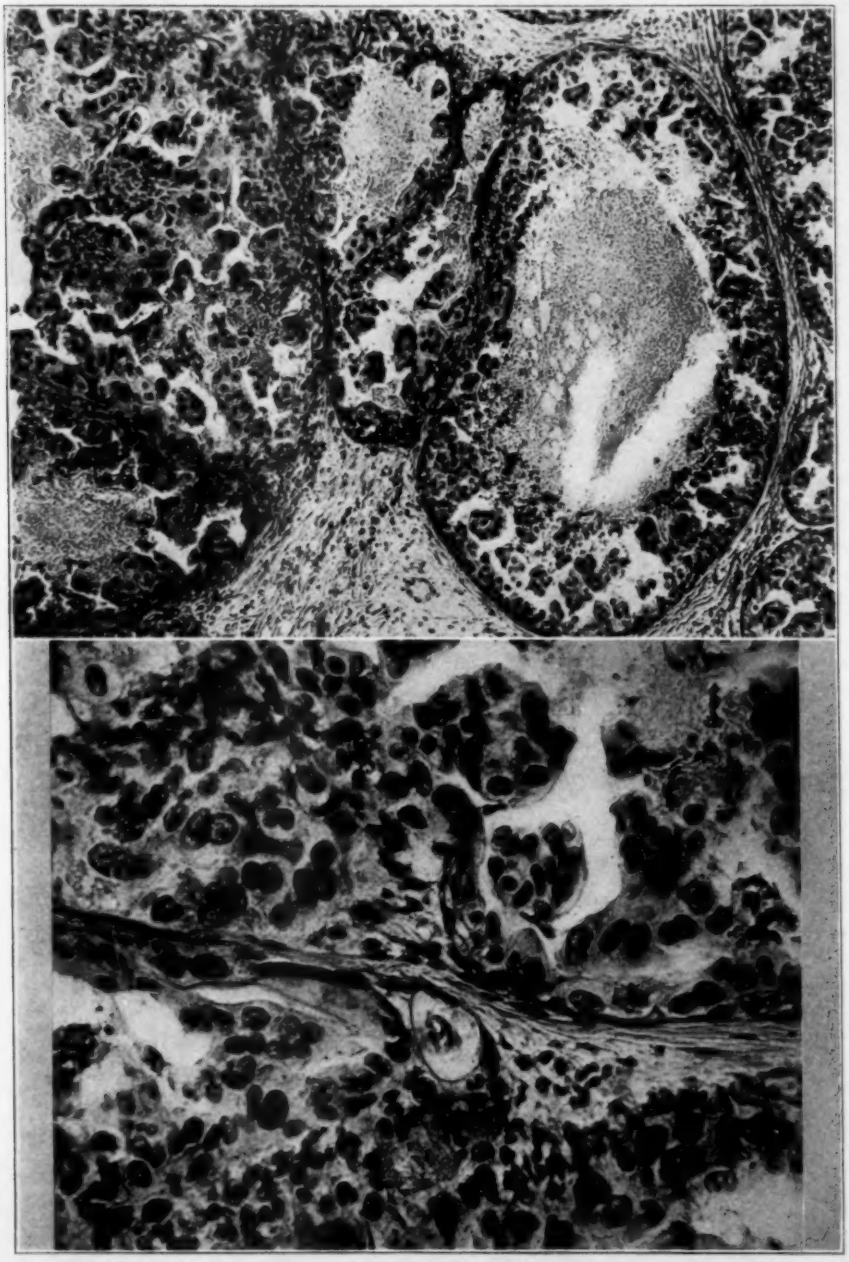

Fig. 7.—Medium and high power photomicrographs of a duct carcinoma, showing large malignant cells similar to those seen in Paget's disease of the nipple. This type differs from the comedo carcinoma in clinical course and in prognosis.

Fig. 8.—Photomicrograph showing an area of a comedo carcinoma occurring in an adenocarcinoma.

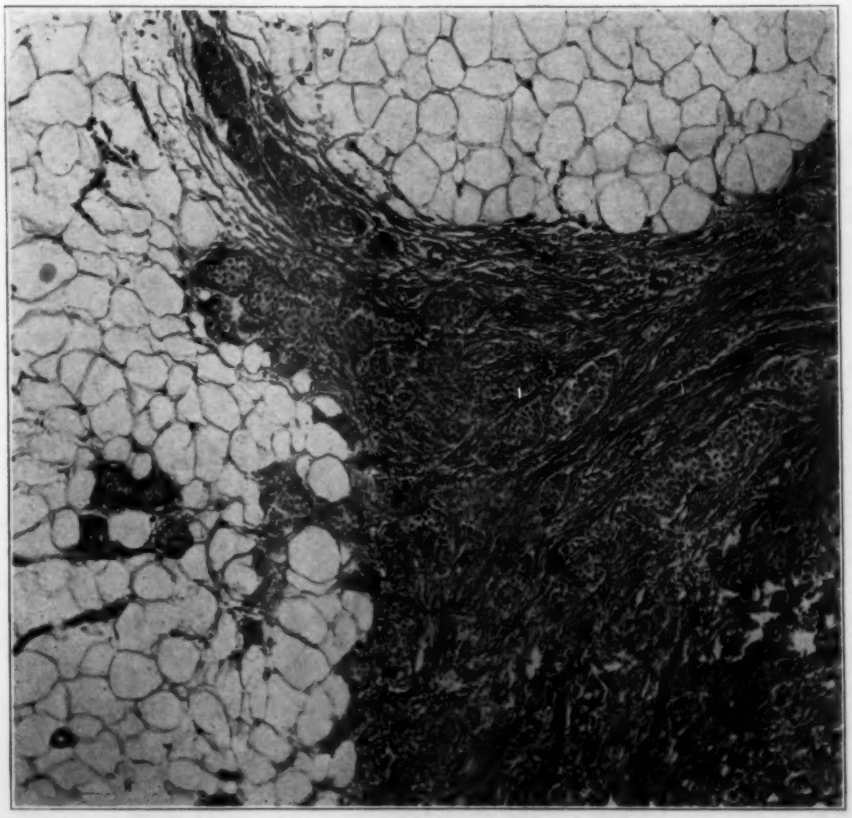

Fig. 9.—Photomicrograph showing an area of a scirrhous carcinoma in the same growth presented in figure 8.

islands of scirrhous carcinoma is a prominent feature (figs. 8 and 9) which allows this growth to be differentiated microscopically from comedo cancer.

Many of the cases in the literature described as instances of duct cancer are examples of slowly growing adenocarcinoma developing in intraductal papilloma. Although arising within the confines of the ducts, the epithelium giving rise to such a tumor has acini-forming potentialities and gives rise to adenocarcinoma rather than to comedo carcinoma.

CEREBRAL PNEUMOGRAPHY

VENTRICULOGRAPHIC INTERPRETATION OF TUMORS IN AND ABOUT THIRD VENTRICLE, AQUEDUCT OF SYLVIUS AND FOURTH VENTRICLE

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IOWA CITY

I. GENERAL CONSIDERATIONS

Since the introduction of cerebral pneumography by Walter E. Dandy,[1] many works bearing on the interpretation of the pneumogram have been forthcoming.[2] The use of the pneumogram in diagnosis indeed made it possible to transform what would be for many patients an exploration of the brain into an exploration of the pathologic condition of the brain. The pneumograph is an instrument of precision, and as such its safety and usefulness will be proportional to specialized knowledge and experience. The day has passed for criticism of pneumography on the basis of its inherent dangers. When one compares the tragic nature of intracranial disease requiring surgical intervention with the treasured information that pneumography provides, the latter has no danger.

I have adopted the policy of attempting to fill the ventricular spaces completely with air, so as to obtain as complete a ventriculogram as possible under the circumstances. Moreover, I do not limit the procedure

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1. Dandy, W. E.: Ventriculography Following the Injection of Air into the Cerebral Ventricles, Ann. Surg. **68**:5, 1918; Roentgenography of the Brain After the Injection of Air into the Spinal Canal, ibid. **70**:397-403, 1919.

2. (*a*) Torkildsen, Arne, and Penfield, Wilder: Ventriculographic Interpretation, Arch..Neurol. & Psychiat. **30**:1011-1021 (Nov.) 1933. (*b*) Dyke, C. G., and Davidoff, L. M.: The Demonstration of Normal Cerebral Structures by Means of Encephalography: I. The Choroid Plexuses, Bull. Neurol. Inst. New York **2**:331-346, 1932; The Demonstration of Normal Cerebral Structures by Means of Encephalography: II. The Corpora Quadrigemina, ibid. **3**:138-146, 1933; The Demonstration of Normal Cerebral Structures by Means of Encephalography: III. The Cerebral Convolutions and Sulci, ibid. **3**:147-189, 1933. (*c*) Locke, C. E.: Studies of Casts of the Cerebral Ventricles, Arch. Neurol. & Psychiat. **15**:588-596 (May) 1926. (*d*) Penfield, W. A.: Cerebral Pneumography, ibid. **13**:580-591 (May) 1925. (*e*) Grant, F. C.: Ventriculography, S. Clin. North America **8**:927-940, 1928.

to cases of so-called silent tumor, but prefer it as a preliminary measure in certain cases in which neurologic examination provides data of localizing value. From a surgical standpoint it is often not enough to localize a tumor roughly by means of the neurologic information. Not only may the neurologic information be grossly misleading, but it may encourage the surgeon to explore somewhat eccentrically the bulk of a tumor. He then finds it necessary to widen an already extensive craniotomy incision for adequate exposure. The close similarity in the neurologic findings between a tumor of a cerebellar hemisphere and one in the contralateral frontal lobe is commonly known. A large meningeal fibroblastoma may cause symptoms and signs which are inadequate for the preparation of the optimum exposure. The two following cases are illustrative of this situation:[3]

REPORT OF CASES

CASE 1.—E. S., a white woman aged 46, complained of diminished visual acuity and headache, which had been present for six months. She had spells of jerking of the right hand and arm during which she would appear dazed but would nod when spoken to. She was beginning to have strange ideas. Bilateral papilledema and bitemporal hemianopia were present. At times there appeared to be a loss of cortical sensation on the right. A roentgenogram of the skull revealed questionable changes in the midsagittal, posterofrontal region. A ventriculogram verified these changes, for it showed a bilateral filling defect of the anterior horns and part of the body of both ventricles (fig. 1 *A*). On the diagnosis of a meningioma about the sagittal sinus a suitable osteoplastic flap was prepared, and a meningioma bilateral to and invading the sinus, weighing 120 Gm., was removed (fig. 1 *B*). It was necessary to remove a segment of the sagittal sinus 2½ inches (6.3 cm.) long. The patient fully recovered and is oriented and able to do her own housework.

CASE 2.—M. S., a white woman aged 48, had had weakness of the left arm and leg for nine months and blurred vision for one month before examination. During the last month she had had convulsions of the left arm and leg, which spread to the left side of her face.

Examination revealed bilateral papilledema with diminished visual acuity and a slight bitemporal cut in the visual fields. There were hemiparesis and diminished cortical sensation on the left side. A roentgenogram revealed a questionable erosion at the vertex of the skull. A ventriculogram showed a filling defect of

3. Dr. Clarence Van Epps, Professor of Neurology, cooperated in this study by referring a large group of patients to me. Many of the routine procedures presented were performed by members of the departments of ophthalmology, otolaryngology, roentgenology and pathology.

the body of the left ventricle and a depressed right ventricle (fig. 2*A*). On the diagnosis of a bilateral meningioma about the sagittal sinus, a suitable exposure was made over the vertex, which adequately uncovered a meningioma bilateral to and invading the sagittal sinus. The tumor was removed without undue trauma to the brain (fig. 2*B*), but when the sinus was ligated posteriorly to the tumor the patient failed rapidly and died on the operating table.

An intraventricular tumor or a tumor deeply situated may, by pressure on the parietal lobe, cause signs referable to the motor or sensory cortex. If the surgeon has incontrovertible evidence of the presence

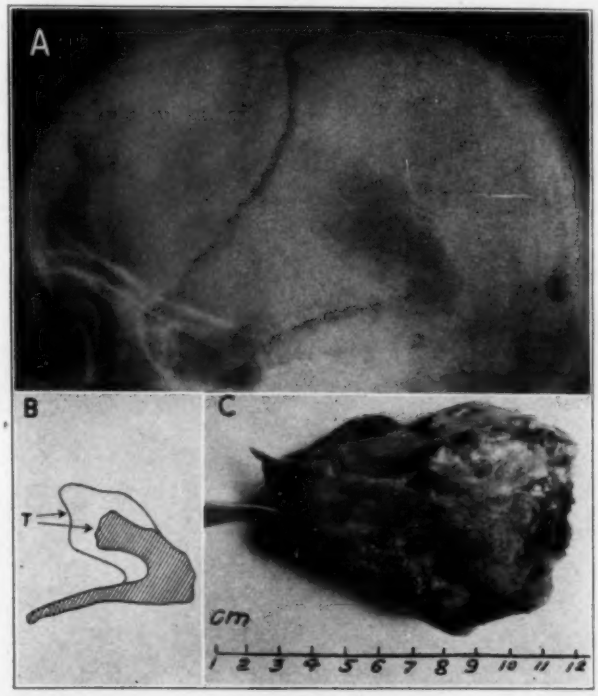

Fig. 1 (case 1).—*A* shows a ventriculogram demonstrating a filling defect in the anterior aspect of both ventricles. The bone is eroded at the vertex of the skull. *B* is a diagrammatic representation of the ventricles. The shaded portion represents the left ventricle, and the unshaded portion represents the right ventricle. The margin of filling defect due to the tumor is indicated by *T*. *C* shows a meningeal fibroblastoma. The hemostat is attached to one end of the segment of the sagittal sinus which has been removed.

and location of such a tumor, he is provided with the necessary courage and justification for carrying his exploration to the pathologic process.[4]

4. Dandy, Walter E.: Benign, Encapsulated Tumors in the Lateral Ventricles of the Brain: Diagnosis and Treatment, Baltimore, Williams & Wilkins Company, 1934.

A tumor situated largely in one of the so-called silent regions may cause neurologic signs as a result of pressure on nearby structures or as a result of edema remote from the tumor. In such an instance the optimum exposure will not necessarily be one centered over the anatomic counterpart of the signs. While it is true that edema remote from a tumor will distort the ventricles, localization of the tumor will ordinarily not be difficult.

Occasionally, accepted signs will falsely indicate the side on which the pathologic condition is situated.

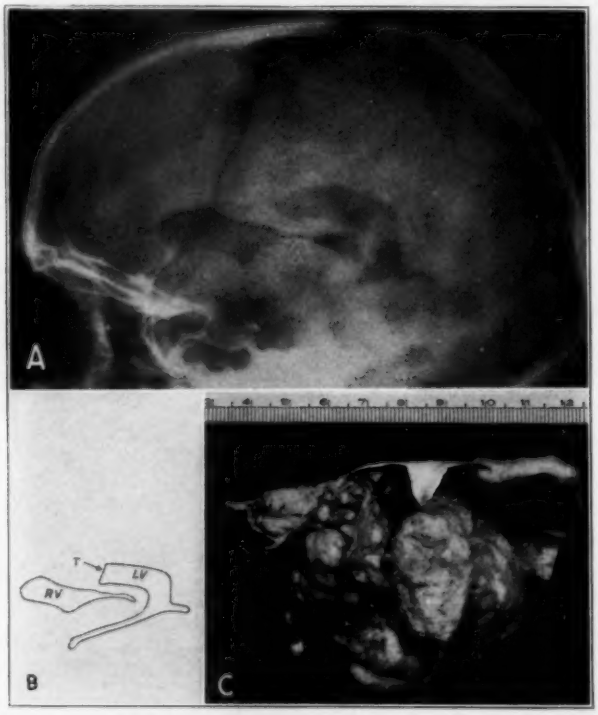

Fig. 2 (case 2).—*A* shows a ventriculogram demonstrating depression of the right ventricle and obliteration of the anterior aspect of the left ventricle. The skull is eroded in the region of the vertex. *B* is a diagrammatic representation of *A*. The right ventricle is indicated by *RV*, and the left ventricle by *LV*. *T* indicates the margin of filling defect due to the tumor. *C* shows a meningeal fibroblastoma. Note the cross-section of sagittal sinus which is infiltrated with the tumor in the upper left. The scale is in centimeters.

Case 3.—J. K., who was thought to have a chronic subdural hematoma, presented increased intracranial tension, a stiff but weakened right arm and a dilated left pupil. These signs indicated a lesion on the left side. A preliminary ventriculogram prevented a serious surgical error, for the hematoma was in the right frontal region.

CASE 4.—A. R., a young girl, presented a syndrome of increased intracranial tension, headache, vomiting and choked disks, indicating a tumor. A roentgenogram of the skull revealed a partially destroyed sella turcica with evidence of "snow flake" calcification above it. So definite was the indication of the presence of a tumor that a right subfrontal exploration was made for a supposed tumor of Rathke's pouch. Subsequently a ventriculogram revealed clearly a tumor in the left lateral ventricle. The destruction of the sella was a false localizing sign, and subsequent study left no doubt that the apparent calcification was actually due to the tumor. The growth proved to be an ependymoma.

In short, I believe, with all due respect to the neurologic examination, that experience must be replete with inadequate, ill controlled and unhappy explorations. It is felt that these could be minimized greatly by more extensive and more complete ventriculographic studies as a preliminary measure to exploration. Rather than regarding the procedure as a danger which should be avoided, I feel that it is an obligation to the patient that all the most precise information obtainable be had in order to expedite a well directed and cleancut attack on the pathologic condition.

An experience with some two hundred and fifty ventriculograms has been successful except in possibly two cases. The case of one patient, D. C., is outlined in the case reports (case 25), and the report of the other case follows:

CASE 5.—E. B., a middle-aged white woman, presented increased intracranial tension and marked papilledema. There had been a rapid mental change, and the patient was not "en rapport" with her surroundings. The neurologic examination did not reveal sufficient data for localization, but it was felt that she had a destructive frontal tumor. A ventriculogram was made by replacing 30 cc. of ventricular fluid with an equal amount of air. There was absence of air in the anterior horn and in part of the body of the left ventricle (parts 1 and 2).[5] The entire remaining system was shifted markedly to the right (fig. 3 *A*). The picture augmented the feeling that there was an extensive glioma in the left frontal region, and preparation was made for exploration to be done the following morning. It was late to begin a craniotomy, and the air was allowed to escape from the ventricle through a ventricular needle. The patient's condition did not seem ominous except for wide variations in blood pressure from hour to hour. She suddenly ceased breathing at midnight. Necropsy disclosed a meningeal fibroblastoma the size of a golf ball situated in the anterior-inferior-mesial aspect of the left frontal lobe and arising from the falx (fig. 3 *B*). There was extensive edema of the white matter on the left throughout the entire anteroposterior diameter. This edema accounted for the great proportion of the filling defect and displacement of the ventricular system. A frontal tumor had been inferred, however, and if the patient had been operated on the tumor would no doubt have been disclosed.

I formerly entertained the idea that extensive edema of the white matter, as demonstrated in the case just reported, is not to be expected,

5. This designation is in conformity with that proposed by Torkildsen and Penfield.[2a]

with a benign tumor. If this were true, it would be of value, in that when the whole hemicerebrum, ventriculographically speaking, seemed to be involved, the evidence would be in favor of an infiltrating tumor. The extensive shift of the ventricular system would thus be due in a large measure to swelling of the white matter. With the feeling that

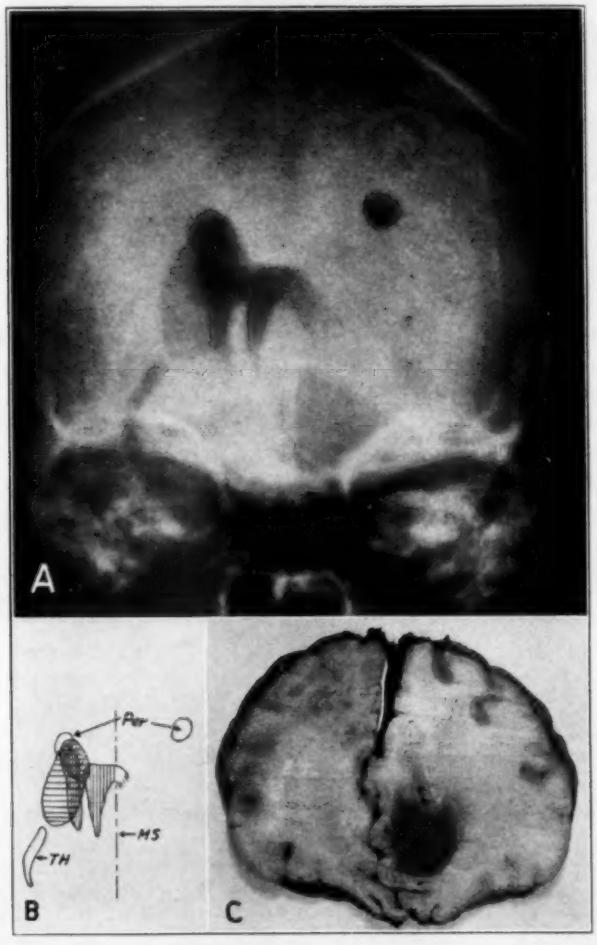

Fig. 3 (case 5).—*A* shows the anteroposterior view of a ventriculogram, demonstrating a marked shift of the system to the right and obliteration of the left anterior horn. *B* is a diagrammatic representation of *A*. The horizontal cross-hatch is the right anterior horn, the vertical cross-hatch represents parts 2 of the ventricles,[2a] and the stipple is part 3 of the right ventricle. The right temporal horn is indicated by *TH*, the midsagittal plane by *MS* and the perforator openings by *Per*. *C* is the section of the brain which is anterior to the ventricles showing the meningeal fibroblastoma. The tumor is not shown in its greatest diameter. Attachment to the falx was more anteriorly placed. There is extensive edema of the white matter of the left hemisphere, which existed in the entire anteroposterior diameter of the left hemisphere.

such was the case in this patient, I did not wish to perform an emergency craniotomy at midnight. The observations at necropsy demonstrated clearly that such a hypothesis is not tenable and emphasized again the dictum that the ventriculogram cannot be expected to give information concerning the nature of the tumor. The surgeon who makes a practice of foregoing an exploration because he believes the pathologic condition inoperable will surely be confronted from time to time at necropsy with one of the most regrettable tragedies of neurosurgery, i. e., a lesion for which something could have been done. The following cases illustrate the impressive results from failure to incorporate ventriculography:

CASE 6.—M. W., a white woman aged 53, complained of right hemiplegia, increased intracranial tension, choked disks and aphasia. The aphasia was interpreted as of the motor type because both cortical and ordinary sensation were shown to be intact in the right hand. When objects were rubbed in the hand the patient could indicate that stereognostic sense was not lost. It was felt that the neurologic evidence was sufficient to postulate a tumor in the left frontal region; consequently the usual osteoplastic flap was turned down in the left fronto-parietal area. The patient did not do well from the time the incision was begun, though she improved a little when the dura was opened. Release of fluid from the small ventricles provided little relief from the marked increased tension. A deep incision in the frontal lobe disclosed the anterior pole of a meningioma situated in the mesial-superior aspect of the parietal region and arising from the falx. The content of the capsule was soft and partly degenerated, so that a portion could be quickly sucked away. The poor condition of the patient demanded that further procedure be abandoned. The wound was closed, and a subtemporal decompression was left. The patient died several hours later. A study of the brain left no question in my mind that if a ventriculogram had been made preliminary to operation a far more adequate approach would have been indicated (fig. 4). It is conceivable that the tumor could have been dealt with successfully even considering the narrow margin of safety within which I had to work.

CASE 7.—A year ago I operated on a young boy, A. H., who had shown rapid development of symptoms of tumor, consisting of vomiting, markedly increased intracranial tension and choked disks progressing to blindness. There appeared to be marked ataxia and disparity of muscle tone on the two sides, which left little doubt as to the cerebellar localization of the tumor. However, ventricular trephinations were made preparatory to exploration, and a ventricular needle was placed in each posterior horn. Fluid was obtained at a depth of 2 cm. on each side, and the dilatation of the ventricles was so marked that when fluid was injected in one side a free flow was obtained from the other side. The disillusion was a result of pressure, since the ventricles did not communicate, but this partial ventricular estimation only confirmed the previous diagnosis and a cerebellar exploration was needlessly carried out. A ventriculogram later revealed an unmistakable tumor which filled the anterior aspect of the left lateral ventricle and blocked both foramina of Monro (fig. 5 *A*). The tumor was a cystic astrocytoma, which was partially removed (fig. 5 *B*).

Occasionally when passing the ventricular needle into the brain one will be fortunate enough to strike a cyst. In such an instance it

is well to inject some air after the fluid has ceased to flow. Roentgenograms will then give precise information concerning the location of the cyst.

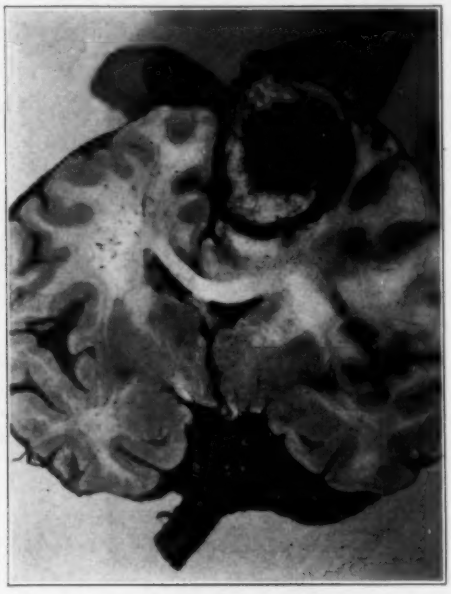

Fig. 4 (case 6).—A meningeal fibroblastoma is shown on the left. From the appearance of the ventricles it is logical to suppose that a ventriculogram would have indicated a more accurate and direct exposure than did the neurologic findings.

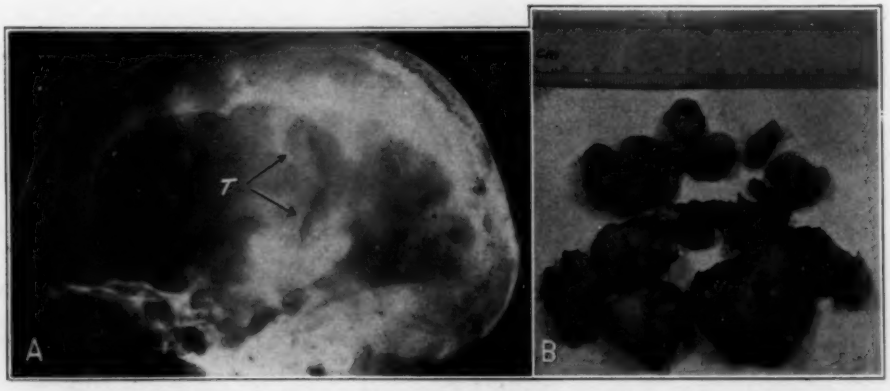

Fig. 5 (case 7).—*A* shows a symmetrical hydrocephalus except for the filling defect, *T*, in the anterior aspect of the left lateral ventricle. *B* shows portions of the mural tumor (astrocytoma) that were removed.

Case 8.—V. O., a white woman aged 19, presented symptoms of tumor consisting of headaches, vomiting, dizziness, bilateral choked disks and spinal fluid pressure of 20 mm. of mercury in the prone position. There were no signs of

localizing value. When a needle was passed toward the right posterior horn a cyst was entered and yielded about an ounce (28 cc.) of thick glairy yellow transparent fluid, which proved to contain 167 mg. of cholesterol per hundred cubic centimeters. The fluid was replaced with 10 cc. of air. The left posterior born was easily entered, and 15 cc. of ventricular fluid was replaced with an equal amount of air. The roentgenograms were interesting and conclusive and revealed a large cyst in the right parietal region which came very close to the surface of the cortex just under the parietal boss (fig. 6). The ventricular system was shifted to the left. A small craniotomy was prepared directly over the cyst, and through an incision in the capsule of the cyst a walnut-sized mural nodule was completely excised with the cautery knife. The cyst proved to be histologically similar to an astrocytoma, although not typical. Recovery was uneventful, the disks receded and the dynamics of the cerebrospinal fluid was restored to normal.

While the foregoing remarks have expressed the importance of a more extensive use of general ventriculography, I wish to illustrate

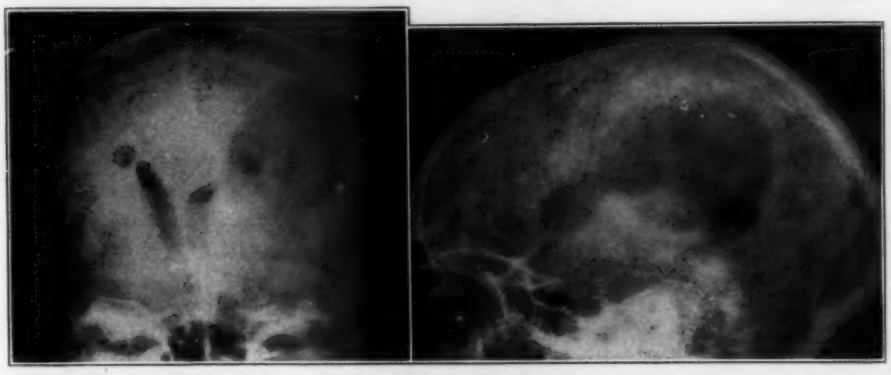

Fig. 6 (case 8).—The ventriculograms were made in the anteroposterior and left lateral positions and demonstrate a cyst and the ventricular system independently. A small craniotomy directly over the cyst sufficed for the complete removal of a pedunculated mural tumor (astrocytoma).

the importance and value of a complete ventriculogram, particularly in view of differentiating tumor in or about the third ventricle, tumor of the pineal body, tumor anterior or posterior to the aqueduct and subtentorial tumor. The widely different exposures for a suprasellar tumor, a tumor of the third ventricle, a tumor of the pineal body and a subtentorial tumor make their differentiation most important. Often the presence of a tumor in the sagittal plane distal to the foramina of Monro can be elicited only by ventriculography, but more important is the fact that the different types of tumors cannot be differentiated from one another unless the ventriculogram is complete. The indirect evidence afforded by symmetrically dilated lateral ventricles without a satisfactory attempt to obtain visualization of at least the third ventricle is inadequate and leaves the surgeon in doubt as to his choice of exposure.

In three instances when the ventricular injection proved unsatisfactory, I immediately supplemented this with a small spinal injection

of air and obtained satisfactory visualization. When the intracranial pressure has been reduced to atmospheric pressure or, as in these three cases, if an open ventricular needle is left in the ventricular system, such a procedure is not felt to be particularly hazardous. Two cases, those of L. S. and A. McD. (cases 14 and 23), in which a supplementary spinal injection was done are outlined in the case reports, and the other case was one of essential hypertension with marked increased intracranial tension. A ventriculogram revealed normal lateral ventricles, which in such an instance might justly be taken as sufficient information, but a normal third ventricle, aqueduct of sylvius and fourth ventricle were clearly demonstrated by a supplementary spinal injection.

Normal ventriculograms do not contraindicate the presence of a tumor. Patients whose ventriculograms are normal will, however, usually come to the physician because of symptoms and signs other than those attributable to the usual tumor. The histories of these patients and the results of neurologic examination overrule a normal ventriculogram, and many such cases constitute the instances of early tumor of which the neurosurgeon dreams. I have observed three such cases within the past eighteen months. One, that of J. H., is discussed in the case reports (case 11).

Following are descriptions of two cases of tumor in which there were normal ventriculograms.

CASE 9.—W. C., a 23 year old white man, presented a history of petit mal seizures of increasing frequency and severity which had been present for nine years. The history and the seizure pattern indicated the anatomic substratum to be that of the right frontal lobe, particularly the rig' + frontal adversive field. The ventriculogram and the intracranial pressure wer normal, but a diagnosis of a nondeforming astrocytoma of the right frontal lobe was made. This was verified at operation, and a resection of the lobe was rewarded with complete cessation of seizures. (There has been no recurrence at the time of this report, eighteen months later.)

CASE 10.—L. I., a woman aged 40, presented a short history of migraine-like headache and brief seizures consisting of flashes of colored light in the left visual field, associated with transient ataxia of the left arm and leg. There was a small homonymous cut in the left visual field. The intracranial pressure and the ventriculogram were normal. Exploration was carried out, and 1½ inches (3.8 cm.) of the right occipital lobe was resected. When the tissue was sectioned, an angioma about 1 cm. in diameter was disclosed. The angioma was situated in the midregion of the area striata and showed evidence of old repeated hemorrhages in its vicinity (fig. 7).

FACTORS CONCERNED IN THE TECHNIC AND MANAGEMENT OF VENTRICULOGRAPHY

1. I prefer to make an incision with a perforator over each posterior horn with the patient in the cerebellar position. Incisions ¾ (1.8 cm.) to 1 (2.5 cm.) inch long are made in a sagittal plane about 1 inch

from the midsagittal plane and beginning about 1 inch superior to the superior nuchal line. In this operation as well as in all intracranial operations it is felt that a most meticulous preparation of the scalp is important. The head is shaved by a barber on the morning of the operation, and in only rare instances is there a compromise as to the amount of hair to be sacrificed. The assistant reshaves the head in reverse direction, scrubs the scalp with soap and water thoroughly and follows this with solutions of alcohol and ether. In the operating room the field is prepared by a wide margin with 7 per cent tincture of iodine, which is allowed to dry and then removed with several sponges of

Fig. 7 (case 10).—Mesial aspect of the right occipital pole. *P* indicates the parieto-occipital fissure; *C*, the calcarine fissure; *A*, an angioma present in the calcarine fissure. The hemostat points in the tip of the posterior horn.

alcohol. Double thicknesses of towels are securely fastened to the scalp with high grade sharp safety pins by the gloved hand. Wide drapes are subsequently anchored to the pins. (For ventricular trephines the towels alone are used in conjunction with a sheet over the patient's body.) It is my opinion that the preparation and draping of the operative field are a weak link in intracranial operations, and postoperative infections are more likely to have their source from an inadequately prepared field than from a break in technic on the part of the surgeon. By strictly adhering to the foregoing methods, I have been fortunate enough to have experienced only two postoperative infections in some

three hundred intracranial operations. The source of one of the infections was a leak of the cerebrospinal fluid, while that of the other infection was an incisional hematoma improperly managed.

Anesthesia other than a local injection of a 2 per cent solution of procaine hydrochloride is seldom needed, even for small children. The incisions are spread by means of a three prong self-retaining mastoid retractor. A shallow beveled perforator is used, and the inner opening of the trephine is rounded off with a suitable blunt instrument so as to expose an area of dura about ⅛ inch (0.3 cm.) in diameter. Only the dura is incised with a pointed scalpel, and the incision is spread with the blunt point of a ventricular needle. A single silk suture in the galea and several deep sutures in the skin suffice for the closure. The patient is transferred to a cart and is controlled by an assistant; the patient is placed on his side with his head lying on a sand bag. The suspected normal side is placed dependently. After a loose draping of sterile towels, the dependent ventricle is entered. By means of a rubber tube connector, a three way stopcock and an easy-working 20 cc. syringe, the injection of air is made.

2. In consideration of the contrast medium used for visualization of cerebral topography, gas is at present far superior to any other known medium. I prefer to use atmospheric air, since no serious objection to its use relative to other gases has ever been presented and the working equipment is reduced to a simple outlay.

A complex apparatus for spinal injection of air has recently been devised that is deserving of consideration.[6] The apparatus is designed to replace the cerebrospinal fluid with gas by a continuous flow. The machine is mechanically ingenious and novel in performance. Disadvantages in the operative procedure are unnecessary additional apparatus, the necessity of two lumbar punctures and the fact that performance depends on free unhampered flow of cerebrospinal fluid, which often does not obtain. The high quality of the pneumogram, which is attributed to the apparatus, is undoubtedly due to the mechanical courage of the apparatus in making a complete injection rather than to any inherent property of the machine.

3. The question often arises as to how much air is injected into the ventricles. This obviously depends on the capacity of the ventricles. An attempt is made to replace all of the available fluid with air in the case of either ventricular or spinal injection. Fluid is replaced by air in quantities of 5 to 10 cc. One should avoid creating a negative pressure by suction or an excessively increased pressure by force, but I do not believe it important that an increased intracranial pressure be maintained.

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6. von Storch, T. J. C.: On Technique of Encephalography with Special Reference to Use of Apparatus, Am. J. Roentgenol. **35**:78-92, 1936.

From a purely physical standpoint, the amount of fluid evacuated is more important than the amount of air injected. A small amount of air under atmospheric pressure will diffuse itself in every space provided by the evacuation of fluid, but gas under increased pressure cannot be expected to replace fluid that remains. Nor does the roentgen ray penetrate and consequently reveal air under pressure with any greater efficiency. Consequently I usually leave the completely drained ventricles filled with air under approximately atmospheric pressure, and I often accomplish this by leaving the needle open for a moment before it is withdrawn. It might be proposed that a reduction of increased tension during the procedure is hazardous, particularly when one is dealing with a tumor that tends to expand and bleed, such as the glioblastoma, but such untoward reactions have not occurred; moreover, the craniotomy that is likely to follow will accomplish the reduction to atmospheric pressure in any case.

The complete emptying of the ventricles is aided by systematic rotation of the head and finally by removing the sandbag so that the head may be tilted laterally. This procedure encourages emptying of the third and fourth ventricles. The initial injection is purposely limited to one side until an anteroposterior roentgenogram is developed. Failure of communication to the opposite side constitutes valuable information, and in such an instance the opposite ventricle is injected independently.

The fact that the lateral ventricles communicate does not necessarily indicate patency of the foramina of Monro. Dilated ventricles are frequently associated with a perforated septum pellucidum. Two findings, however, may be accepted as accurate evidence: (1) Failure of air to pass from one lateral ventricle to the other is positive evidence that the foramen of Monro is obstructed, at least on the side of the injection, and (2) if air does or does not communicate between the two lateral ventricles and the injection has been complete enough to give good visualization of both ventricles on the same roentgenogram in the lateral positions, but without visualization of the third ventricle, there exists obstruction of both foramina of Monro or the third ventricle itself. It is in such a case that a supplementary spinal injection of air in selected cases may outline the distal margin of a tumor and thus guide the surgeon in his important choice of exposure.

It requires only twenty to thirty minutes as a rule to prepare the trephines and complete the injection of air. Six roentgenograms are made as a routine: of an anteroposterior view, a postero-anterior view and a stereoscopic view in each lateral position.

Some neurosurgeons inject only a limited amount of gas and depend on a shift of the "gas bubble" to obtain visualization. Four additional roentgenograms are made: a stereoscopic view with the brow slightly elevated and a view with the occiput slightly elevated in each lateral

position. Unless enough fluid is replaced by air so that when the patient is in the lateral position there is more than enough air to fill the upper ventricle, obviously the third ventricle will not be visualized.

4. The ideal situation is one in which the operation is performed as soon as the roentgenograms are developed and interpreted. This should ordinarily not require more than twenty minutes from the time the roentgenograms are made. It is needless to say that the surgeon should be skilled in interpreting the ventriculograms. It is imperative in neurosurgery, more than in any other field of surgery, that all data and information concerning the problems be encompassed in a single mind in order to attain that which is difficult but possible.

I have yet to be confronted with an untoward reaction if the ventricles have proved to be normal, but with the presence of a tumor that has not been operated on: the postventriculographic period may be disturbing. Postponement of the operation until the following day is a gamble against heavy odds. Ventriculography in the event that a tumor is found should be regarded as a part of the major operation. which should be carried to some conclusion at the earliest possible moment. The fact per se that air is injected into the ventricles is of little consequence, but the inevitable disturbance of relationships of tension that have been so precariously balanced between the tumor and its environment is of extreme importance.

If for some reason the craniotomy is postponed, the patient should be given special nursing care and frequent records should be taken of the pulse, respiration and blood pressure. A fluctuating blood pressure is an ominous sign of endangered vital centers.

If the ventricles are not greatly dilated and all channels are open for free circulation of cerebrospinal fluid, the air will be absorbed satisfactorily without intervention. It is my opinion that the absorption is accomplished by solution of the gas in the cerebrospinal fluid. The gas is then carried into the blood stream in a state of solution. If the ventricles are greatly dilated, increasing tension may manifest itself beginning one or two hours after the injection. In this case air should be allowed to escape through a ventricular needle by repeated punctures if necessary.

If there is some obstruction in the circulation of cerebrospinal fluid, air may remain in the ventricles indefinitely and be the cause of a febrile reaction and increased tension. In such a case it is imperative that the air be removed by the surgeon.

There will aways be a percentage of cases of tumor of the brain of such a nature that death will be inevitable whether the patient is operated on or not. This outcome cannot always be predicted, however, except in retrospect. Death in such instances may occur for no other reason than the fact that a high tension has suddenly been released to

atmospheric pressure. There follows an overwhelming expansion of tumor and brain, with damaging results that are beyond the most skilful operator's control. Death will occasionally follow a simple subtemporal decompression, for the same reasons. Would that such an outcome could always be accurately predicted and a timely policy of noli me tangere adopted. Such vision, however, is possessed only by the occult. In neurosurgery the sins of omission may be quite as culpable as the sins of commission. Too conservative a policy in this light, at least until the pathologic condition has been unequivocably established, is not to the best interest of patient or medical profession. In short, from the unfortunate legion of supposed hopeless patients some may be greatly benefited, and this fact should be the guiding spirit of the neurosurgeon. It is not the deaths from the irretrievable pathologic condition that sting the surgeon's conscience, but the denial of succor to those who were retrievable. It is my opinion that the percentage of irretrievable patients has contributed largely to high ventriculographic mortalities, and it is not good scientific judgment to hold the diagnostic method in unconditional disrepute.

VENTRICULOGRAPHIC INTERPRETATION OF TUMORS IN AND ABOUT THE THIRD VENTRICLE, AQUEDUCT OF SYLVIUS AND FOURTH VENTRICLE

A CHARACTERISTIC DEFORMITY OF THE SYLVIAN AQUEDUCT DUE TO TUMORS OF THE VERMIS

It is not within the scope of this paper to discuss in detail the pathologic nature and the symptomatology of the types of tumor dealt with except so far as the dependability of clinical methods of localization of the tumors is concerned.

It is possible to localize a high percentage of suprasellar neoplasms from the clinical and roentgenologic findings. The important tumors in the suprasellar region are those of the hypophysial stalk, the suprasellar meningiomas and tumors arising from the chiasm. Martin and Cushing [7] reported that 3 to 8 per cent of all suprasellar neoplasms are primary gliomas of the optic chiasm or of the intracranial portions of the optic nerves, and they may simulate clinically the tumors of the hypophysial duct.

Beckman and Kubie [8] pointed out that suprasellar meningioma almost never occurs before 30 years of age. These authors reported a series of twenty-one cases of tumor of the hypophysial stalk in which a cor-

7. Martin, P., and Cushing, H.: Primary Gliomas of the Chiasm and Optic Nerves in Their Intracranial Portion, Arch. Ophth. **52**:209-241 (May) 1923.

8. Beckman, J. W., and Kubie, L. S.: A Clinical Study of Twenty-One Cases of Tumor of the Hypophyseal Stalk, Brain **52**:127-171, 1929.

rect diagnosis was made on the clinical and roentgenologic findings in all but three cases. Endocrinologic and neurologic signs may vary considerably. Primary atrophy of the optic nerve and bitemporal defects of the visual fields are extremely valuable indications of suprasellar tumor in adults. For patients in adolescence or preadolescence, however, it is often impossible to obtain visual fields, and the marked papilledema often associated with a suprasellar cyst may nullify the importance of moderate defects in the fields. In Beckman and Kubie's cases, papilledema and hydrocephalus occurred only in adolescence.

Another feature pointing strongly to the diagnosis of suprasellar cyst is the changes seen in and above the sella in the roentgenogram. McKenzie and Sosman [9] and Cushing [10] pointed out that suprasellar or intrasellar opacities are seen in 70 to 80 per cent of the cases.

There is a certain percentage of cases, however, in which the diagnosis will be indefinite. This is true of two of the cases which are to be reported, those of J. H. and G. T. (cases 11 and 13). It is possible but rare that a diagnosis of a suprasellar tumor will be falsely indicated, as in the case of A. R. discussed earlier in the paper (case 4).

Bailey [11] has pointed out that a suprasellar tumor can produce cerebellar symptoms. Hence in cases in which a diagnosis is not definite or possible, an adequate ventriculogram is in order, which will reveal the tumor.

A discussion of tumors of the thalamus is included in this paper because they produce filling defects in the third ventricle. A thalamic syndrome has been described,[12] but ventriculographic evidence is most welcome. In the case of J. P. (case 15), exploration was indicated. It is conceivable that the tumor may be a benign tumor of the third ventricle pressing on the thalamus, although I have been unable to find a report of such a growth which was accompanied with Roussy's thalamic syndrome. An extremely interesting case in which there were autonomic seizures has been reported by Penfield.[13]

It may be said that tumors of the pineal body, corpora quadrigemina and third ventricle present symptoms that not only are largely due to hydrocephalus but are often so closely allied that differentiation of the

9. McKenzie, K. G., and Sosman, M. C.: The Roentgenological Diagnosis of Cranio-Pharyngeal Pouch Tumours, Am. J. Roentgenol. **11**:171-176, 1924.

10. Cushing, H.: The Intracranial Tumours of Preadolescence, Am. J. Dis. Child. **33**:551-584 (April) 1927.

11. Bailey, P.: Concerning the Cerebellar Symptoms Produced by Suprasellar Tumours, Arch. Neurol. & Psychiat. **11**:137-150 (Feb.) 1924.

12. Roussy, G.: La couche optique (étude anatomique, physiologique et clinique), Thèse de Paris, no. 165, 1907.

13. Penfield, Wilder: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358-374 (Aug.) 1929.

tumors is only a guess.[14] More important is the fact that a subtentorial tumor, especially one in the vermis, is likely to be confused with the tumors just mentioned. Unfortunately, the clinical evidence of a pineal tumor is not always present or dependable. The literature is extensive and fairly complete concerning the pathologic nature of tumors in these locations as well as the clinical signs and symptoms presented by patients the nature of whose tumors was confirmed at autopsy.[15] In summary, however, the whole chapter resolves itself into the fact that tumors of the third ventricle, pineal body, quadrigeminal plate and vermis will seldom lend themselves to a definite clinical differential diagnosis. In a majority of the cases reported the attempt at diagnosis provided opportunity for only a fascinating neurologic exercise, the answer to which was sought at necropsy.

Tumors of the quadrigeminal plate are inoperable, and the importance of the pneumogram lies in the attempt to rule out the presence of a tumor of the third ventricle or a pinealoma.

The literature concerning cerebellar symptomatology is almost too extensive to cover fully, and the fact is not questioned that symptoms and signs often exist that betray a tumor of the cerebellum. Two facts remain, however: First, a tumor of the vermis or fourth ventricle can be silent except for obstructive hydrocephalus; second, given an obstructive hydrocephalus and even a ventriculogram showing dilated lateral ventricles without visualization of the third ventricle, a cerebellar exploration will be done by choice. A tumor proximal to the aqueduct will be missed, and often an opportunity to make a second attack will be denied because death supervenes. A routine cerebellar exploration will be successful in most cases of obstructive hydrocephalus because the incidence of cerebellar tumors is higher, but the other group of tumors must not be abandoned. The brilliant possibilities of surgical intervention on the third ventricle and the pineal body cannot be utilized unless diagnoses are accurately made. The only adequate method of diagnosis is complete ventriculography, this being a method of certainty.

Benign tumors in the third ventricle constitute one of the most fascinating chapters in cerebral neoplasia. Whether the patient is granted a full normal life or a miserable death often depends on the removal of a small cyst or tumor, usually no larger than a pecan. The correct diagnosis of such a tumor and the operative attack offer a challenge of the highest order to the neurosurgeon, and the successful

14. Glaser, M. A.: Tumours of the Pineal, Corpora Quadrigemina and Third Ventricle, the Inter-Relationship of Their Syndromes and Their Surgical Treatment, Brain **52**:226-262, 1929.

15. Fulton, J. F., and Bailey, Percival: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1-25, 134-165 and 261-277, 1929.

extrication of the tumor is a conquest of unmatched reward. It is here that technical ideals in neurosurgery reach a high point, for one is dealing with a lesion that is dangerous not by reason of its pathologic nature, but by reason of its position, which makes it incompatible with life. That the cyst or tumor can be successfully removed in a high percentage of cases is now an established fact, and thus is added another brilliant chapter to neurosurgery.[16] The diagnosis will always constitute a brilliant achievement in each individual case. I feel that a successful diagnosis can be made consistently by using ventriculography to its fullest advantage.

A masterly treatise on benign tumors in the third ventricle has been prepared by Dandy.[17] It deals with the situation from the diagnostic, operative and pathologic standpoints. The importance of the complete use of ventriculograms is emphasized. In four cases of the twenty-one which he reported, Dandy passed up a nonvisualized third ventricle to perform a cerebellar exploration, but he found it was necessary to retrace his steps and finally uncover the tumor through a third ventricle approach.

Formerly, symmetrically dilated communicating lateral ventricles were considered sufficient indication for a cerebellar exploration, and errors of making such explorations were considered excusable. To explore the cerebellum now without having made every effort to visualize the third ventricle is to neglect adequate diagnostic methods.

From a pathologic standpoint benign tumors of the third ventricle are classified as follows: colloid cysts, which comprised five of the twenty-one of the tumors in Dandy's series and which probably arise from the ependymal epithelium; a heterogenous group of tumors, comprising circumscribed ependymal gliomas, pearly tumors as reported by Penfield,[13] simple cysts and papillomas of the choroid plexus, and an unclassified group of circumscribed grossly benign tumors which it is thought arise from undifferentiated cell rests.

Tumors of the pons are inoperable, and I have never made a ventriculogram in a case of such a growth. The diagnosis may be suspected owing to early and advanced clinical signs, but in case of doubt it is logical to suppose that the aqueduct of Sylvius would be shifted backward and its normal curvature emphasized.

Ventriculography has relatively little importance in the diagnosis of tumors of the eighth nerve, since the clinical syndrome is definite.

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16. McLean, A. J.: Paraphysial Cysts, Arch. Neurol. & Psychiat. **36**:485-513 (Sept.) 1936. Masson, C. B.: Complete Removal of Two Tumors of the Third Ventricle with Recovery, Arch. Surg. **28**:527-537 (March) 1934.

17. Dandy, Walter E.: Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

McConnell and Childe,[18] however, have filled the gap here with the report of a case of tumor of the eighth nerve in which a lateral displacement of the aqueduct was shown in the anteroposterior and the postero-anterior roentgenograms. A part of the splendid paper by McConnell and Childe is devoted to ventriculographic interpretation of tumors of the third and fourth ventricles.

The operative finding of so-called cystic arachnoiditis with obstruction of the foramina of Luschka and Magendie will often leave the surgeon in doubt as to whether this cystic arachnoiditis is the extent of the pathologic condition.[19] Even a dilated fourth ventricle should not necessarily preclude the presence of a partial obstruction proximally placed. Hydrocephalus causing a degree of herniation of the cerebellar tonsils through the foramen magnum could secondarily cause an adhesive arachnoiditis about the foramen of Magendie. A ventriculogram which shows no filling defect to the foramen of Magendie will dispel any such doubt.

THE THIRD VENTRICLE, AQUEDUCT OF SYLVIUS AND FOURTH VENTRICLE, AS SEEN IN THE NORMAL VENTRICULOGRAM

The relations of the third ventricle, the aqueduct of sylvius and the fourth ventricle are shown in figure 8 *A*. The structures which can usually be visualized in the ventriculogram are the foramina of Monro, the optic and pituitary recesses, the massa intermedia, the suprapineal recess, the pineal recess, the aqueduct of Sylvius and the fourth ventricle. In a normal ventriculogram the shadows are definite but less dense than the shadows in a ventriculogram showing dilated ventricles.

Figure 8 *B* is a normal ventriculogram in which all the structures are clearly seen except the optic and pituitary recesses. In the films made in the cases reported here, the optic and pituitary structures were more clearly demonstrated. In the normal ventriculogram the suprapineal recess and the pineal recess are usually pointed shadows, but they round off and become emphasized in a ventriculogram showing a dilated third ventricle. The suprapineal and the pineal recess are usually both present, but occasionally one or the other may be absent. The suprapineal recess is an important landmark because it marks the posterior extremity of the third ventricle. The distance of the shadow of the suprapineal recess

18. McConnell, Lorne H., and Childe, Arthur E.: Pneumographic Localization of Tumors of the Brain: Tumors of the Lobes of the Cerebrum, Arch. Neurol. & Psychiat. **37**:33-55 (Jan.) 1937; Tumors Involving the Basal Ganglia, Lateral Ventricles, Brain Stem and Cerebellum, ibid. **37**:56-67 (Jan.) 1937.

19. Horrax, G.: Generalized Cisternal Arachnoiditis Simulating Cerebellar Tumor: Its Surgical Treatment and End-Results, Arch. Surg. **9**:95-112 (July) 1924.

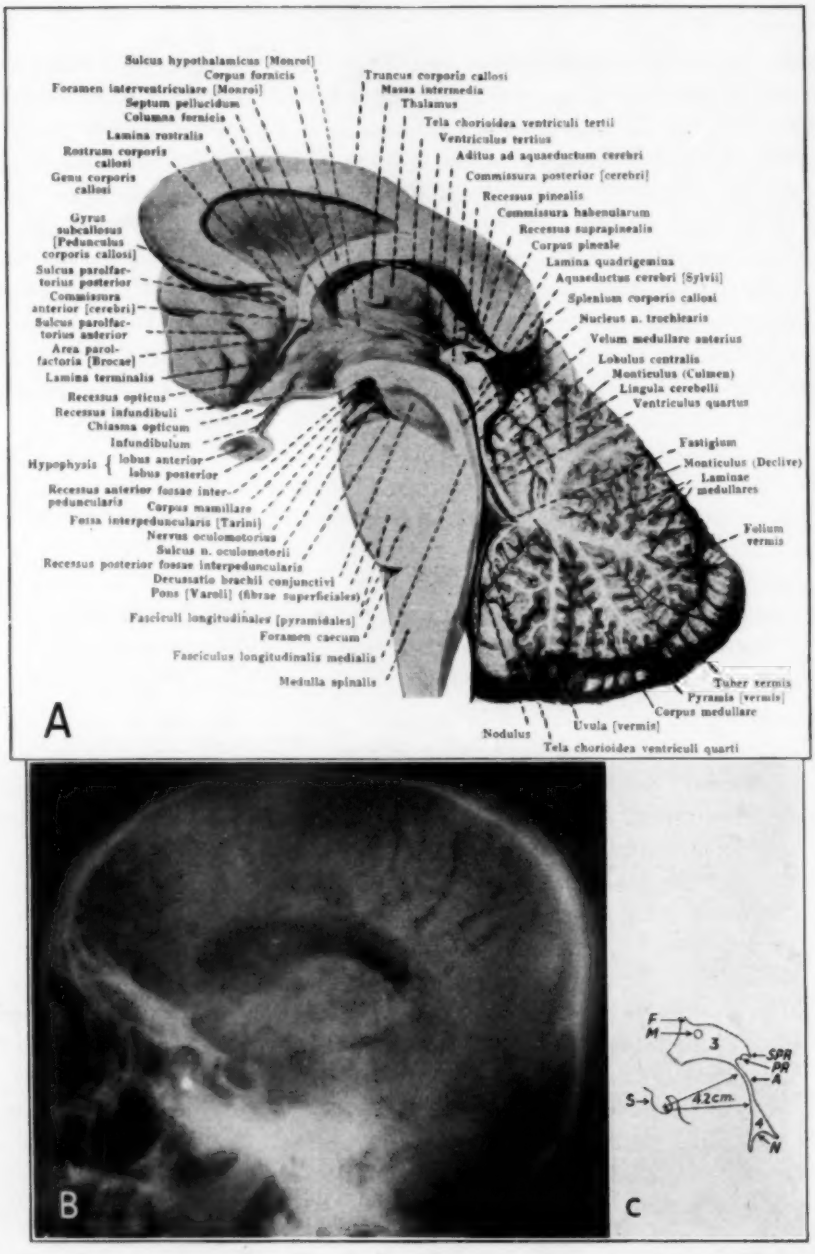

Fig. 8.—*A* (taken from K. W. Spalteholz: Hand Atlas of Human Anatomy, Philadelphia, J. B. Lippincott Co., 1900-1903) demonstrates the relations of the normal third ventricle. *B* shows a normal ventriculogram. *C* is a diagrammatic representation of the third ventricle, aqueduct and fourth ventricle seen in *B*. *F* indicates foramen of Monro; *M*, massa intermedia; *3*, third ventricle; *SPR*, suprapineal recess; *PR*, pineal recess; *A*, aqueduct of Sylvius; *4*, fourth ventricle; *N*, invagination of the fourth ventricle due to the cerebellar nodulus; *S*, sella turcica.

from the negative shadow of the massa intermedia is roughly about three to four times the distance of the shadow of the massa to the anterior margin of the shadow of the third ventricle. The recess is due to a herniation of the tela choroidea and the epithelial lining of the ventricle backward, over and lying on the pineal body. The size of the recess may vary considerably in the normal brain. Thus an unusually large recess is demonstrated in figure 9. The patient had markedly increased intracranial tension and died of malignant hypertension. The ventriculogram was normal. A postmortem examination of the brain revealed generalized edema with occlusion of many arterioles by intimal thickening. There was evidence of a small hemorrhage in the left temporal lobe.

Fig. 9.—*A* is a normal ventriculogram showing an unusually large suprapineal recess. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *A*, proximal segment of the aqueduct of Sylvius. *C* shows a section of the brain demonstrating the large suprapineal recess. A section has been removed, including the pineal body. The posterior reflection of the tela choroidea is drawn in.

The normal aqueduct is seen as a pencil-like shadow about ¾ inch (1.9 cm.) long, showing a smooth curve the convexity of which is directed backward. The radial center of the curve is the midpoint of the floor of the sella (fig. 8*B*). This radius in the original ventriculogram measured 4.2 cm.

The fourth ventricle widens into a triangular structure with a curve invaginating its base. This curve varies somewhat from case to case and outlines the cerebellar nodulus.

REPORT OF CASES

TUMOR IN OR ABOUT THE THIRD VENTRICLE [20]

CASE 11 *(Suprasellar Cyst).*—J. H., a man aged 34, was referred to the department of ophthalmology in August 1935 by Dr. Mark C. Jones, of Boone, Iowa. The patient complained of diminishing visual acuity and headache, which had been present for several months. Bright lights hurt his eyes, and there were burning and smarting when he attempted to read. Headaches were of daily occurrence, lasted from one to three hours and were augmented by jarring or stooping. The headaches were usually in the right temporofrontal region. There was no nausea or vomitnig. Examination revealed a visual acuity of 6/21 in the left eye and 6/21 in the right. The visual fields showed a bitemporal hemianopia. The patient was transferred to the department of neurology, where an encephalogram was made (fig. 10). There was good filling of the ventricles and subarachnoid spaces in the anteroposterior view, and they were regarded as normal. (The third ventricle did not show in the lateral view.) The patient was transferred to the neurosurgical service, however, since it was thought that the findings in the visual fields were more significant than the negative encephalogram.[21] The chiasm and the suprasellar region were explored by the right subfrontal route.[22] Preparatory to elevation of the frontal lobe, a ventricular needle was passed toward the anterior horn. When the stylet was withdrawn, 10 cc. of opalescent yellow fluid came forth, and without the needle's being moved this fluid was followed by clear cerebrospinal fluid. The yellow fluid subsequently proved to contain 310 mg. of cholesterol per hundred cubic centimeters. The suprasellar region revealed nothing abnormal, and with the evidence at hand I did not feel justified in sectioning the right optic nerve for a more thorough exploration. The subsequently proved content of cholesterol in the yellow fluid led me to believe strongly, but not conclusively,[23] that I was dealing with a posteriorly placed suprasellar cyst which had probably contracted from view when its contents were evacuated. The patient's headaches were relieved, and his visual acuity was greatly improved. He was discharged temporarily, but he returned in two months with severe headaches and greatly diminished vision. A complete ventriculogram revealed unmistakable evidence of a suprasellar mass (fig. 11), and even though on reexploration the cyst was still not evident, I felt justified in sectioning the right optic nerve. A posteriorly placed cyst with a capacity of about 10 cc. was

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20. Only positive findings are discussed in the case histories and examinations.

21. Here the pneumogram cannot be termed strictly "negative," because I did not visualize the third ventricle in the lateral view. Had the third ventricle been visualized, there is no question but that it would have presented the same pathognomonic deformity that was subsequently demonstrated.

The encephalogram is used to denote spinal insufflation of air, while the ventriculogram denotes insufflation of air directly into the ventricles. This universally accepted connotation of the two terms is unfortunate, however, for spinal injection of air may lead to both an encephalogram and a ventriculogram.

22. Heuer, G.: Surgical Experiences with an Intracranial Approach to Chiasmal Lesions, Arch. Surg. **1**:368-381 (Sept.) 1920; Surgical Approach and the Treatment of Tumors and Other Lesions About the Optic Chiasm, Surg., Gynec. & Obst. **53**:489-518, 1931. Adson, A. W.: Hypophysial Tumors Through the Intradural Approach, J. A. M. A. **71**:721-726 (Aug. 31) 1918.

23. I have had five cases of cystic astrocytoma in which the fluid contained a high percentage of cholesterol.

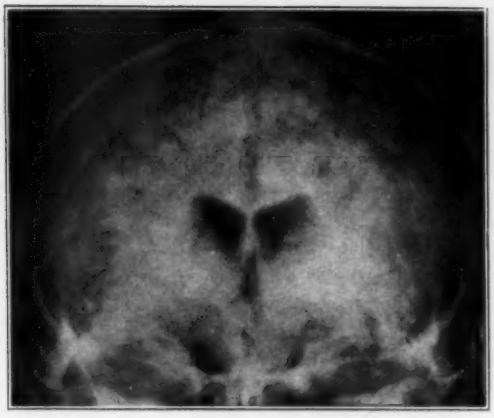

Fig. 10 (case 11).—This ventriculogram was made by spinal injection of air and was regarded as normal in the anteroposterior view shown. The lateral view taken at the same time did not reveal the third ventricle (fig. 11).

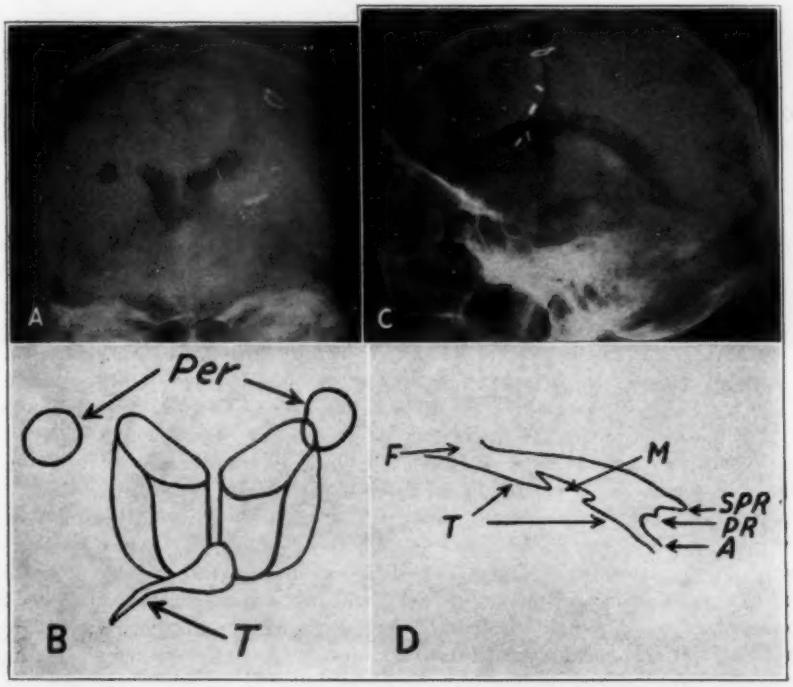

Fig. 11 (case 8).—*A* shows a ventriculogram taken two months after the ventriculogram shown in case 8 (fig. 10). *B* is a diagrammatic representation of *A*. *T* indicates a marked shift of the third ventricle seen in the anteroposterior view, and *Per* indicates perforator openings. *C* is a lateral view showing a filling defect in the anteroinferior aspect of the third ventricle. *D* is a diagrammatic representation of *C*. *F* indicates foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *PR*, pineal recess; *A*, aqueduct of Sylvius; *T*, margin of filling defect due to suprasellar cyst.

brought into view and entirely removed. The patient recovered uneventfully. It is interesting to note that when a light shone toward the nasal side of his left retina he consistently experienced the sensation of seeing the light with his right (blind) eye.

CASE 12 *(Suprasellar Cyst)*.—M. J., a white boy aged 5 years, was referred to me by Dr. S. N. Anderson, of Onawa, Iowa, in December 1936. For three months the patient had suffered somnolence, loss of weight, diminution of visual acuity, headaches and staggering gait.

On examination the patient was found to be constantly asleep, but he would arouse somewhat when shaken and give brief answers in a husky voice. He presented a pudgy, somewhat myxedematous appearance, and the skin was noticeably dry. His hands and feet were somewhat spadelike, and his mother informed me that other members of the family had a similar appearance. There were marked bilateral papilledema and paralysis of the right external rectus muscle. The pupils were dilated, of equal size and round and reacted sluggishly to light. The patient refused to walk or to perform most of the usual neurologic tests. The pressure of the cerebrospinal fluid was 250 mm. of water when he was in the prone position. A roentgenogram revealed slight but unmistakable evidence of calcification above the sella, making the diagnosis that of suprasellar cyst. The patient had a slight cough with some nasal discharge, but he was vomiting repeatedly and failing so rapidly that operation without further delay was advisable.

A preliminary ventriculogram was made for the purpose of ascertaining some evidence pertaining to the size of the cyst. If the cyst had proved to be large, aspiration was planned as a preliminary stage. A complete filling of the ventricles was performed, proving free communication between the lateral ventricles but showing complete obliteration of the third ventricle (fig. 12). This indicated the presence of a large cyst, and I had determined to be content at the time with aspiration. A right subfrontal approach was made to the chiasm; a bluish cyst came into view, and 12 cc. of yellow fluid was aspirated. The fluid contained 357 mg. of cholesterol per hundred cubic centimeters. This procedure did not seem to reduce the size of the cyst appreciably, however, and the patient was in such splendid condition under avertin (tribromethanol) anesthesia, which had not necessitated an ether supplement, that the removal of the cyst was begun. It was necessary to section the right optic nerve, after which the usual teasing made it possible to deliver the entire specimen and place a clip on the stalk (fig. 12 *B*). The wound was dry, and the patient was still in a satisfactory condition. His rectal temperature rose to 103 F. in the evening, but it subsequently began to subside. His state of consciousness was encouraging, but his cold became worse. It seemed by the sixth day that there could be no doubt of recovery, but bronchopneumonia developed and the patient died on the seventh postoperative day. Necropsy revealed a dry operative field with no macroscopic damage to the hypothalamus or adjacent structures except for the sectioned optic nerve. There was a perforation in the septum pellucidum about 0.5 cm. in diameter. The cyst had been entirely removed. The lungs revealed bilateral bronchopneumonia.

The tumor proved to be adamantinomatous, and it is of interest that microscopic examination revealed a small amount of infiltration of the tumor into the chiasm. This fact is important in that a suprasellar cyst may be only a part of a tumor of Rathke's pouch and not necessarily a complete entity in itself.

Somnolence was an outstanding feature in this patient's history, as it was in nine of the twenty-one cases reported by Beckman and Kubie.[8]

CASE 13 *(Suprasellar Cyst).*—G. T., a white man aged 19, was referred to the department of psychiatry by Dr. E. S. Kennedy, of Oelwein, Iowa, in December 1935. Four months previous to his first visit the patient and a friend were "bumming" their way home from a trip. The patient became so ill that he purchased a railroad ticket, but his friend continued to ride the freight trains and was killed three days later. The patient felt upset about this, was self accusatory and threatened suicide. When brought to the hospital, he was apathetic, and his responses were limited to "yes" and "no." The eyegrounds appeared normal, and the pressure of the cerebrospinal fluid was normal when he was in the prone position. There was some degree of dehydration. There was marked spasticity of the extremities, the upper extremities being held in partial flexion with the fists clenched. The lower extremities were held extended. The deep reflexes were markedly hyperactive, and the patient winced from painful stimuli. A ventriculogram revealed complete blocking of the foramen of Monro, and it was necessary to fill each lateral ventricle independently.

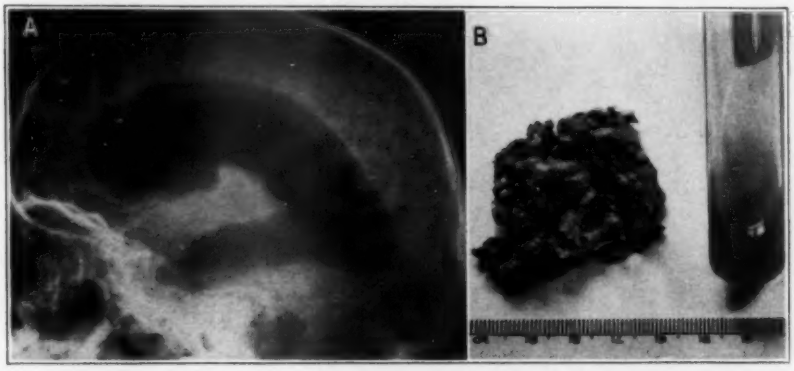

Fig. 12 (case 12).—*A* shows a ventriculogram demonstrating complete absence of the shadow of the third ventricle. The fact that both lateral ventricles are well visualized in the lateral view without visualization of the third ventricle leaves no doubt concerning the obstruction of the latter. Necropsy revealed a perforation of the septum pellucidum 0.5 cm. in diameter. *B* is a photograph of the thick wall of the adamantinomatous cyst after fixation. The cyst had shrunk to about half its original size. The yellow fluid aspirated at the time of operation is shown in the adjacent test tube. The scale is in centimeters.

The third ventricle was never filled, and in the anteroposterior view a filling defect was present in part 2^{2a} of the left ventricle (fig. 13 *A*). A diagnosis of suprasellar cyst was made, with tumor of the third ventricle as second choice. A subfrontal exploration of the suprasellar cyst was advised. Operation was refused, and the patient died. At necropsy a large suprasellar cyst was disclosed which was lined with stratified squamous epithelium. The photograph (fig. 13 *B*) demonstrates how the cyst outgrew its usual confines and by leaning to the left produced the filling defect shown in the ventriculogram.

Beckman and Kubie [8] reported a case of suprasellar cyst in which the patient presented a decerebrate syndrome, and in several of their cases there were upper motor neuron signs.

CASE 14 *(Suprasellar Tumor).*—A. McD., a girl aged 3 years, was referred to the department of pediatrics in July 1935 by Dr. W. L. McConkie, of Carroll, Iowa. The patient complained of diminishing vision, difficulty in walking, an enlarging head, restlessness, nervousness and poor appetite, which had been present for five months.

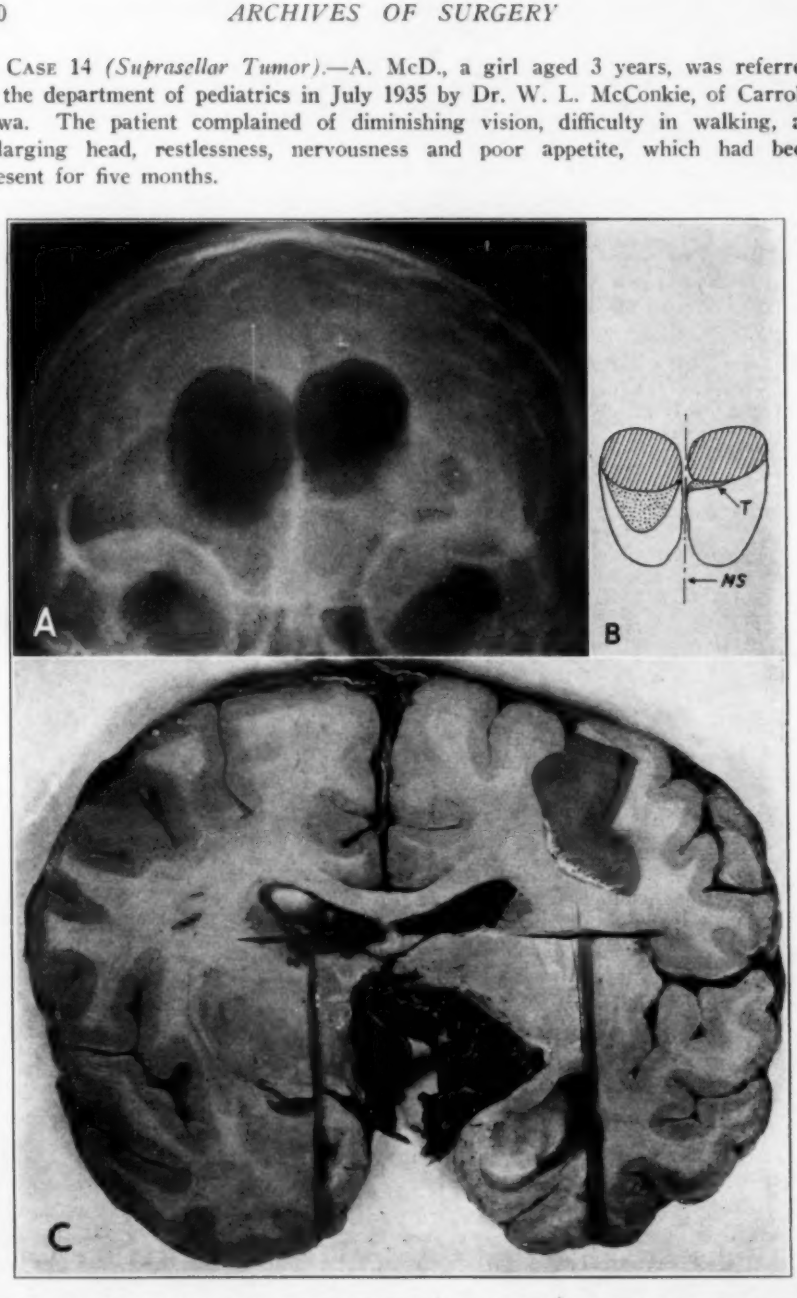

Fig. 13 (case 13).—*A* is a ventriculogram in the anteroposterior view, showing a filling defect in part 2 of the left lateral ventricle and absence of a third ventricle shadow. It was necessary to fill each lateral ventricle independently. Note that the system as a whole is not shifted. *B* is a diagrammatic representation of *A*. *MS* indicates the midsagittal plane, and *T* indicates the margin of the filling defect in part 2 of the left lateral ventricle. *C* is a photograph of the brain demonstrating the large suprasellar cyst.

The patient was 35.7 inches (92.2 cm.) tall and weighed 27 pounds (12.2 Kg.), and the greatest circumference of her head was 50.5 cm. The pupils reacted sluggishly to light, and the optic disks revealed primary atrophy. There was a tremulous movement of the hands and an incoordination of the extremities that resembled cerebellar ataxia. By lumbar puncture the spinal fluid revealed a pressure of 18 mm. of mercury in the prone position and a qualitative increase in globulin. A ventriculogram at first revealed symmetrically dilated ventricles, but the third ventricle was not visualized. Subsequently air was injected into the

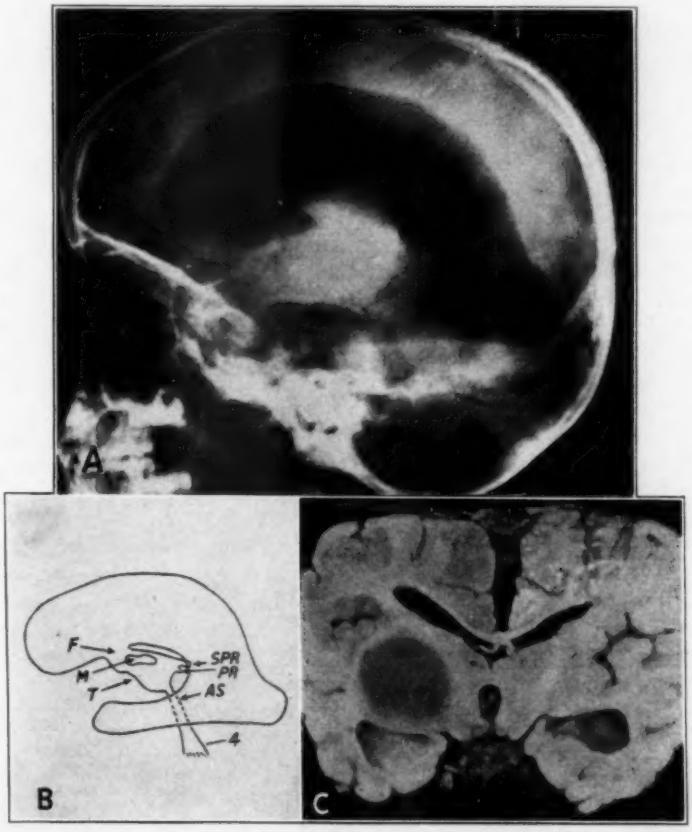

Fig. 14 (case 14).—*A* shows a ventriculogram made by combined ventricular and spinal injection of air. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *PR*, pineal recess; *AS*, aqueduct of Sylvius; *4*, fourth ventricle; *T*, margin of filling defect due to the suprasellar portion of the tumor. *C* is a photograph demonstrating the primary polar spongioblastoma in the region of the right lenticular nucleus.

lumbar theca while a ventricular needle was left in a ventricle. Air bubbled freely through the latter. The ventriculogram now showed the filling defect to be limited to the third ventricle but not completely obstructing it (fig. 14 *A*). The diagnosis was suprasellar tumor, definitely excluding a subtentorial tumor. A right subfrontal exploration of the suprasellar region brought into view a globular

solid subchiasmal tumor firmly attached to the left optic nerve. Since the frozen section revealed what were taken to be spindle-shaped fibroblasts, it was thought to be a tumor arising from the sheath of the optic nerve and was removed without great difficulty. Hyperthermia and rigidity developed, and the patient died on the second day. Postmortem examination revealed the tumor to be a polar spongioblastoma which arose in the right lenticular nucleus and extended in such a way as to form the growth described (fig. 14 *B*).

TUMOR OF THE THALAMUS

CASE 15.—J. P., a Negro aged 38, was referred to the department of neurology by Dr. E. W. Anderson, of Des Moines, Iowa. The patient complained of staggering gait, dizziness, headache, vomiting and diplopia, which had been present for two months. During the past three weeks he had been irrational and disoriented.

On examination there were general tenderness to percussion of the skull, bilateral paresis of the sixth nerve, advanced bilateral papilledema and dehydration. The patient swayed when his heels were together and his eyes closed. There were continued coreo-athetoid movements of the upper extremities; these were at first interpreted as cerebellar ataxia, but the patient performed the usual cerebellar tests well. There were complete astereognosis on the right side and loss of sensation to light touch. He frequently tried to wipe some phantom object from the right palm. There was overreaction to the light scratch of a pin on the right arm, but this was not present on the left arm. The mental reaction was noteworthy because often when spoken to or engaged in conversation the patient would give rational answers but as soon as he was left to himself he would mutter irrationally and call for his sister and mother.

With this precise clinical account, there was no doubt of the presence of the typical thalamic syndrome such as has been outlined by Roussy.[12] However, there was some doubt concerning localization of the tumor, and a ventriculogram was made (fig. 15 *A*). There was a sharply defined filling defect in the posterosuperior aspect of the third ventricle, which was felt to be, in order of probability, a tumor of the thalamus, a tumor of the pineal body, or a tumor in the third ventricle. An interhemispheral approach to the third ventricle was made, and when the splenium of the corpus callosum was divided a vascular infiltrating tumor presented. The patient died several hours after the operation, and necropsy revealed a glioblastoma of the left thalamus (fig. 15 *B*).

TUMOR OF THE PINEAL BODY

I have never had a case of pinealoma, but the ventriculogram would be expected to present obliteration of the suprapineal and pineal recesses and to show a filling defect in the posterior aspect of the third ventricle similar to that seen in the ventriculograms of F. L. and J. L., whose cases are now to be presented. Cases of pinealoma have been reported by Dandy,[24] McLean [26] and McConnell and Childe.[18]

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24. Dandy, Walter E.: Operative Experience in Cases of Pineal Tumor, Arch. Surg. **33**:19-46 (July) 1936; in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1929, vol. 12, pp. 117 and 607.

25. Footnote deleted on proof.

26. McLean, A. J.: Pineal Teratomas with Report of a Case of Operative Removal, Surg., Gynec. & Obst. **61**:523-533, 1935.

TUMOR IN THE THIRD VENTRICLE

CASE 16.—F. L., a girl aged 12 years, was referred to the department of pediatrics in June 1936 by Dr. C. R. Jones, of Atlantic, Iowa. After an attack of influenza in December 1935, the patient began to have frequent attacks of severe generalized headache associated with vomiting. There were blurring of the vision

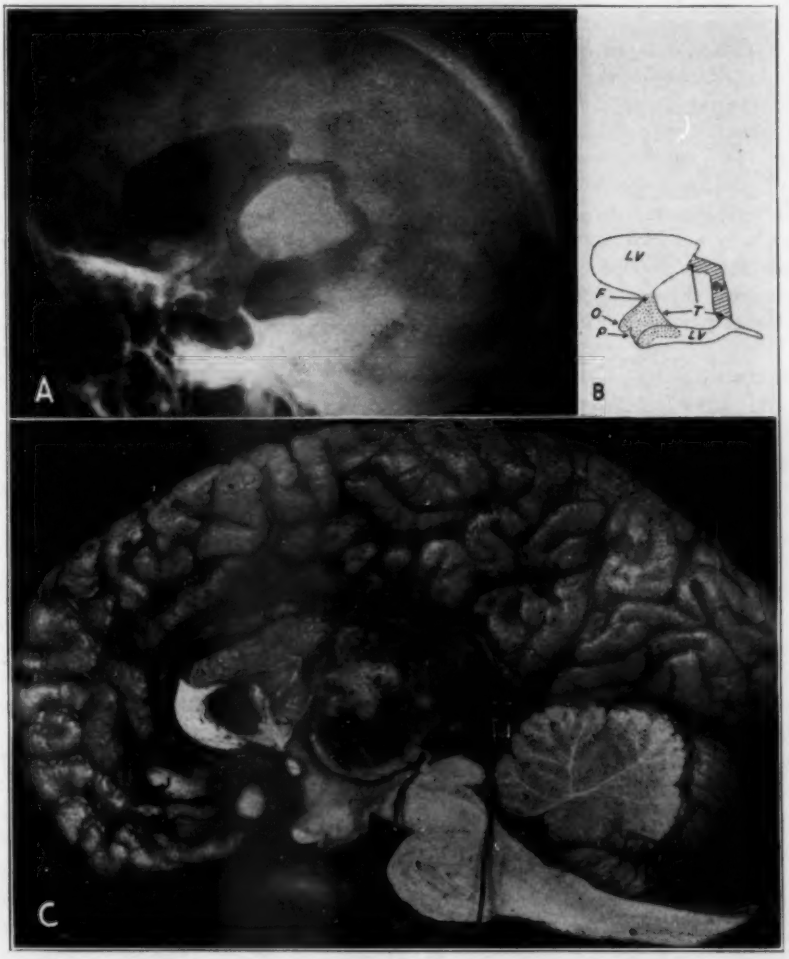

Fig. 15 (case 15).—*A* is a ventriculogram demonstrating a filling defect in the third ventricle and also in the bodies of both lateral ventricles. *B* is a diagrammatic representation of *A*. *LV* indicates left ventricle; *RV*, narrowed body of the right ventricle; *F*, foramen of Monro; *O*, optic recess; *P*, pituitary recess; *T*, margins of the filling defects due to the tumor of the thalamus. The third ventricular shadow is stippled. *C* is a photograph of the brain demonstrating a glioblastoma of the thalamus. A wire is placed through the aqueduct of Sylvius.

and occasional ringing in the ears. At the time of the headaches the patient was often unable to stand and tended to fall backward or to the right. Examination revealed a well nourished, intelligent and cooperative girl with slightly scanning

speech. There was marked secondary atrophy of the optic nerves. The pupils were equal and reacted to light and in accommodation, and the extra-ocular movements were normal, without nystagmus in any direction. There was some stiffness of the neck, and she complained of pain on flexion. There was slight but definite ataxia when the finger to nose test was performed and when she attempted to write. The patient walked unsteadily with a wide base. The reactions to the caloric test, Bárány's test and the audition test were entirely normal. An interesting feature was the fact that the patient always complained of dizziness on turning her head rapidly to one side, though she denied that objects moved or turned before her. While she stood with her heels together and her eyes closed, I turned her head rapidly to one side, and she felt that her feet had rotated in the opposite direction. I flexed her neck, and she felt that her knees had flexed toward her chin. Her answers were not prompted in any way, and the tests were performed again the same day with the same results. I placed some importance on these findings because I have had occasion to observe them in two of Dandy's patients on whom bilateral section of the vestibular nerves had been performed. I was never able to get these responses again in my patient. A week later she did not experience the sensations, but when she opened her eyes after passive turning of her head, objects seemed to rotate in front of her.

While she was in the hospital hyperactive reflexes developed, and the Babinski test elicited a bilateral extensor response. It was felt that she had a tumor of the vermis, and a ventriculogram was made. The lateral ventricles were symmetrical and markedly dilated, but the third ventricle was not visualized. The findings, nevertheless, were considered sufficient evidence for a diagnosis of subtentorial tumor, and a cerebellar exploration was made. The cerebellum was normal. The vermis was incised so that the fourth ventricle could be viewed as high as the lateral recesses. The fourth ventricle was not dilated, and fluid and dye injected into the lateral ventricles failed to appear through the aqueduct. I believed that the patient could have a suprasellar cyst, a tumor of the third ventricle, a pinealoma or a tumor of the quadrigeminal plate; so the wound was closed. The patient improved, and the aqueduct was opened sufficiently to transmit fluid and dye. Two months later ventriculography was repeated. Clinically the patient had acquired a spasticity of the extremities that prevented her from walking. The complete ventriculogram on this second occasion revealed clearly a filling defect in the posterior aspect of the third ventricle, which led me to postulate a pinealoma (fig. 16).

The usual interhemispheral exploration was made. The pineal body was uninvolved, but when the tela choroidea was incised a vascular tumor was disclosed. Dilated vessels were apparently progressing in and out of the posterior wall of the third ventricle, and a plexus was seen coursing down into the sylvian aqueduct. Gentle tugging on this plexus markedly disturbed the patient's respiration, and though the vessels in view were cauterized, further hope of any operative benefit was abandoned. About six hours later the patient suddenly died of circulatory failure. Necropsy was denied, but in the light of the findings it was felt that the tumor may have arisen originally in the quadrigeminal plate and invaded the third ventricle secondarily. However, the tumor may well have had its origin in the choroid plexus, comparable to the tumor described by Dandy.[27] The smooth outline of the anterior border of the tumor as seen in the ventriculogram aroused my suspicion that it was partly cystic in nature. If this was so, I might have incised it when incising the tela choroidea, and then failed to recognize its true nature. A technical point is suggested here, that when the surgeon is exploring

27. Dandy,[17] p. 62.

for such a lesion he should incise the tela choroidea carefully, being on the alert for the thin wall of a cyst adherent to the tela. It is conceivable that one could progress into such a cyst and thenceforth become completely disoriented concerning what would otherwise be a simple lesion.

CASE 17.—J. L., a white man aged 23, was referred to me by Dr. C. E. Chenoweth, of Mason City, Iowa, in December 1936. For four and a half weeks the patient had complained of a sore, stiff neck, double vision and occipital headaches. The neurologic examination gave entirely negative results except for marked bilateral papilledema, fine horizontal nystagmus to both sides and fine vertical nystagmus. Extra-ocular movements and pupillary reactions were normal. The pressure of the spinal fluid was over 400 mm. of water in the prone position. A ventriculogram revealed a symmetrical dilatation of the lateral ventricles and a definite filling defect in the posterior aspect of the third ventricle (fig. 17 *A*). On the diagnosis of a pinealoma or tumor in the posterior aspect of the third ventricle, an osteoplastic flap on the right side similar to that proposed by Dandy

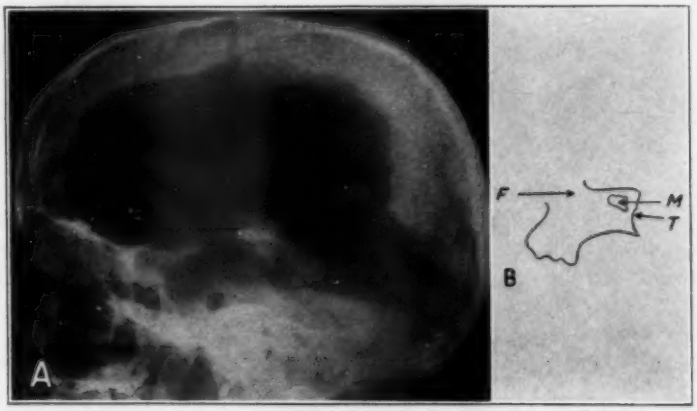

Fig. 16 (case 16).—*A* is a ventriculogram demonstrating a filling defect in the posterior aspect of the third ventricle with obliteration of the supraspinal and pineal recesses. This finding is characteristic of tumors in the posterior aspect of the third ventricle as well as tumors of the pineal body. Both tumors are best attacked through the same surgical approach. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *T*, margin of filling defect due to the tumor.

was designed. This flap allowed an interhemispheral approach to the splenium of the corpus callosum. The latter was incised in the sagittal plane and was of normal thickness. The tela choroidea with its two small veins of Galen came into view and did not appear abnormal. The tela was incised between the veins, and a smooth-walled cyst about 2 cm. in diameter situated in the third ventricle came into view. The cyst was removed easily and intact. Its contents were clear and watery, and the inner lining was corrugated and dark purple (fig. 17 *B* and *C*).

The patient recovered uneventfully, the papilledema subsided and the circulation and pressure of the cerebrospinal fluid were restored to normal. There was no significant color disturbance in the visual fields.

Dr. E. D. Warner, of the department of pathology, described the cyst as follows: "The cyst wall is about 2 mm. in thickness and is composed of glial

EXPLANATION OF FIGURE 17

Fig. 17 (case 17).—*A* is a ventriculogram demonstrating a filling defect in the posterior aspect of the third ventricle similar to one already shown (fig. 16). *B* is a diagrammatic representation of *A*. *F* indicates the foramen of Monro; *M*, massa intermedia; *T*, margin of filling defect due to a benign cyst of the third ventricle. *C* shows reconstructed drawings illustrating the position and relations of the cyst and the operative approach through the splenium of the corpus callosum. *C* indicates cyst; *G*, vein of Galen dividing into the smaller veins; *S*, divided splenium of the corpus callosum; *T*, incised tela choroidea. *D* is a photomicrograph of a cross-section of the cyst wall. *a* indicates the connective tissue capsule and *b* indicates the inner aspect of the cyst, composed of many layers of glial cells.

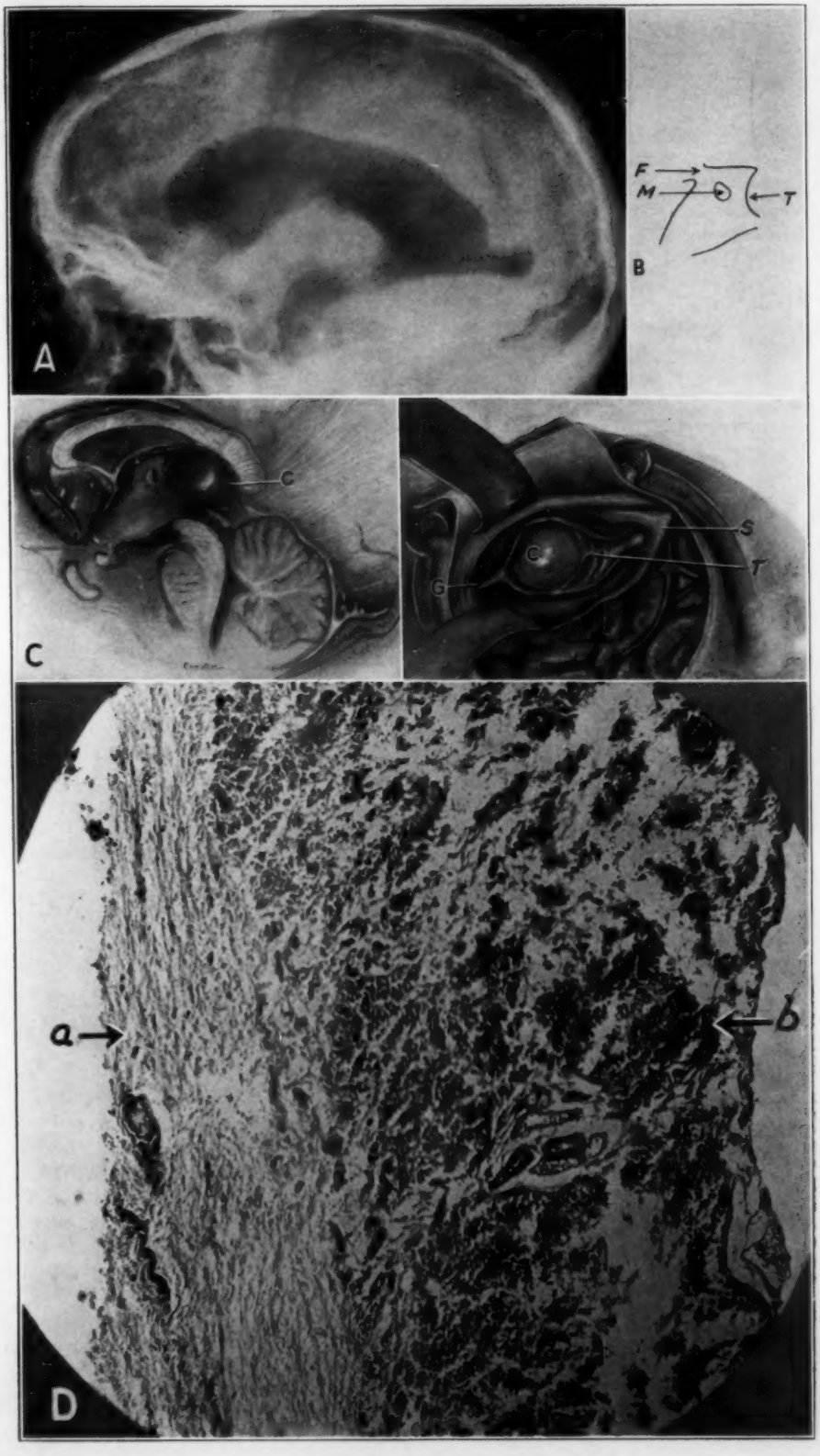

Figure 17

tissue in which fibers are fairly abundant. The cells are closely spaced in some areas, but they are rather uniform in size and no mitoses or giant cells are found. A few phagocytes near the inner surface contain brown pigment. There is no epithelial lining, nor is any colloid material present. The lesion appears to be a gliomatous cyst."

TUMOR OBSTRUCTING THE LATERAL AND THE THIRD VENTRICLE

CASE 18.—O. G., a white boy aged 8 years, wes referred to the department of pediatrics by Dr. Robert Hughes, of Ottumwa, Iowa, in December 1936. For seven months the boy had complained of right frontal headaches, which recently had been accompanied by vomiting. For six months his left leg and arm had become progressively weaker. There was bilateral papilledema of 2 diopters, and the strength and deep reflexes on the left were markedly impaired.

A ventriculogram revealed a perplexing picture, but one which is accurate and worth while analyzing in retrospect. The left lateral ventricle was dilated and was shifted to the left. (Air had been injected into the left posterior horn.) Air progressed through the foramina of Monro, outlining a small portion of the third ventricle anteriorly and showing the margin of a definite filling defect. Only the anterior horn of the right ventricle was visualized (fig. 18). The tumor proved to be a cyst in the posterior aspect of the right frontal lobe. It yielded 30 cc. of clear yellow fluid, which contained 185 mg. of cholesterol per hundred cubic centimeters. A nonpedunculated mural nodule about the size of a walnut was situated in the mesial wall of the cyst in such a way as to block the right ventricle just posterior to the foramen of Monro; in addition, the nodule was compressing the posterior aspect of the third ventricle, producing the filling defect shown in the ventriculogram. The value of the study lies in the fact that filling defects in the third ventricle associated with filling defects in the lateral ventricles indicate tumors that are most likely not intrinsic in the third ventricle.[28] The tumor was extricated, and the patient made an uneventful recovery with complete return to normal.

TUMOR OF THE QUADRIGEMINAL PLATE

CASE 19.—C. H., a white girl aged 9 years, was referred to me in March 1936 by Dr. L. W. Chain, of Dedham, Iowa. When the child was 1 year old it was known that she had a divergent squint. She had always been unsteady when walking and had frequently fallen. She had grown markedly worse during the past six months, so that at the time of examination there was generalized hypotonia with a tendency to remain fixed in any relaxed position. When she was placed on her feet there was marked retropulsion. Her face was expressionless, and after some delay she would give short answers to questions in a rather explosive manner. The voice was bass and hoarse. There were divergent strabismus and fixation with either eye. The pupils were dilated and equal and reacted well to light. The deep reflexes were hyperactive, and all her extremities were ataxic to the usual cerebellar tests. There was astereognosis of the right hand. The intracranial tension was markedly increased so that the patient suffered severe headaches, had projectile vomiting and presented advanced bilateral papilledema.

A ventriculogram revealed ventricles that were markedly and symmetrically dilated (fig. 19 *A*). A small amount of air was visible in the third ventricle, but

28. Dandy, [17] p. 72. Dandy,[4] p. 123. Reference should be made to the report of the thalamic tumor in case 15.

it was insufficient to betray the true nature of the situation. This case was one of the earlier ones, and it was accepted as an instance of subtentorial tumor and exploration was made for such a growth. A more extended effort should have been made to visualize the third ventricle, and this should have been relatively simple since the third ventricle was dilated to the point of obstruction of the aqueduct. This case is included in this paper because postmortem study revealed what the character of a complete ventriculogram should have been (fig. 19 *B*). The possibility of tumor of the third ventricle or pinealoma should have been easily ruled out. The point of obstruction of the aqueduct was high, and while this fact was not conclusive it should have led one to suspect a tumor of the mesencephalon and thus leave less cause for disorientation at the time of operation. As a matter of fact, when the vermis was incised and the enlarged quadrigeminal plate brought into view, the benign appearance of the tumor caused me to suspect strongly a pinealoma. This was the wrong approach by which to attack such a tumor, but I felt that it was important to obtain a small specimen for biopsy in

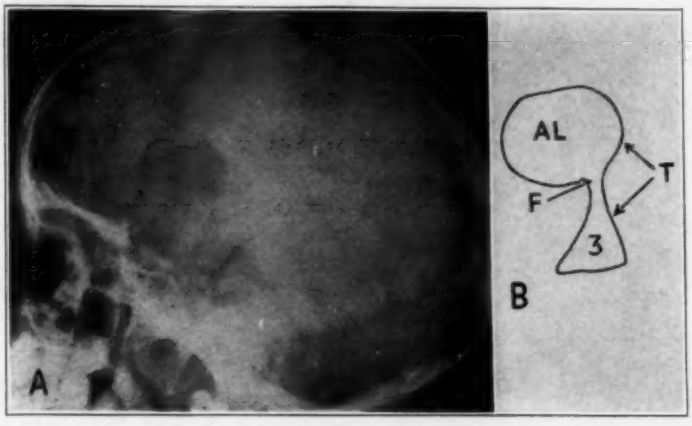

Fig. 18 (case 18).—*A* is a ventriculogram taken in the left lateral position showing only the anterior aspect of the right lateral ventricle and the third ventricle. The view taken in the right lateral position showed a dilated left lateral ventricle without filling defect. *B* is a diagrammatic representation of *A*. *AL* indicates anterior horn (part 1) of the right lateral ventricle; *F*, foramen of Monro; *3*, anterior aspect of the third ventricle; *T*, margins of filling defects due to a mural tumor (cystic astrocytoma).

order to justify a second operation. The operation was thus prolonged, and the trauma to the patient and the agony to the surgeon were unnecessary. The whole query involved the likelihood of pinealoma, which would be the only operable tumor in such a location, and that fact could have been settled with certainty had the third ventricle been thoroughly visualized. Hyperthermia with generalized extensor rigidity developed, and the patient died the second day after operation.

Necropsy revealed a tumor which was almost limited to the superior colliculi. The lumen of the aqueduct was about the size of a horse hair. The pleomorphic nature of the tumor cells led to a pathologic diagnosis of glioblastoma. However, the tumor had evidently been present for a number of years, and it must have been of a more slowly growing unclassified type (fig. 19 *C*).

There are many interesting features concerning this unusual case which I hope to publish in greater detail.

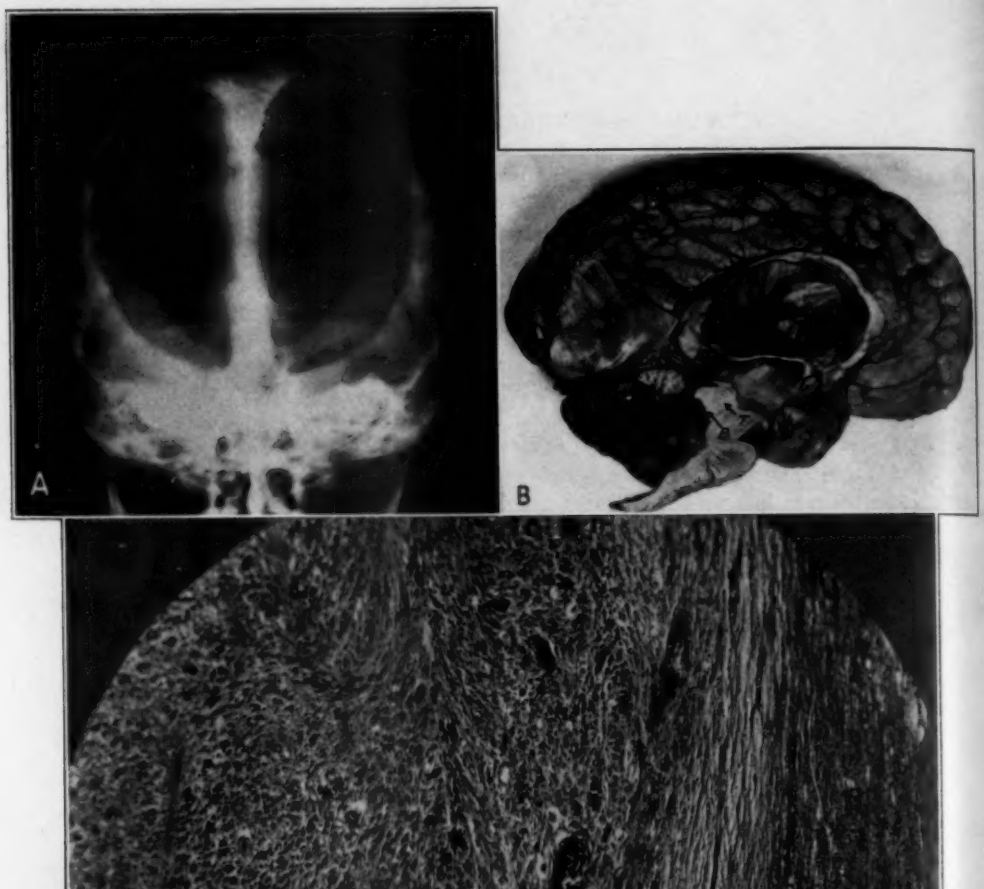

Fig. 19 (case 19).—*A* is a ventriculogram in the anteroposterior view, showing a small amount of air in the third ventricle. The lateral view failed to reveal a third ventricle shadow because the quantity of air injected was not more than enough to fill one lateral ventricle. *B* is a photograph of a brain demonstrating a dilated third ventricle. The appearance of a complete ventriculogram may be deduced from the photograph. I am convinced that if sufficient air had been injected, a more accurate deduction of the nature of the lesion could have been made. *T* indicates a tumor practically limited to the superior colliculi, and *B* indicates the margin of the operative defect from which a specimen for biopsy was obtained. Note the perforated septum pellucidum. *C* is a photomicrograph of the tumor, indicated by *T*, showing its pseudocapsule, *C*.

TUMOR OF THE CEREBELLAR VERMIS

CASE 20.—D. B., a white woman aged 19, was referred to me in July 1936 by Dr. H. A. Lockhart, of Cedar Rapids, Iowa. The patient complained of occipitofrontal headaches, vomiting, failing vision, transient diplopia and stiffness of the neck which had been present for four months. On examination there was bilateral papilledema of 2.5 diopters, and the retinal veins were markedly engorged. The neck was stiff and painful on flexion. The responses to the caloric and Bárány tests were normal. A ventriculogram revealed symmetrically dilated lateral ventricles and showed the outlines of the third ventricle, aqueduct and fourth ventricle in every detail. The lower half of the aqueduct and the fourth ventricle were displaced anteriorly, producing an acute angulation at the junction of the upper third and the lower thirds of the aqueduct of Sylvius (fig. 20 *A*). On the diagnosis of a tumor of the vermis, the usual cerebellar exploration was made. An egg-shaped, thin-walled cyst was disclosed, situated directly between and spreading the cerebellar hemispheres. The vermis was markedly compressed anteriorly (fig. 20 *B*). The parietal layer of the arachnoid was a separate and distinct entity that could be lifted from the cyst, leaving the latter as a transparent, thin-walled structure that contained clear watery fluid. The cyst was easily peeled from its bed, and it seemed to be attached by a frail pedicle arising from the pia on the upper aspect of the right cerebellar hemisphere. The patient fully recovered, and the papilledema receded.

A case similar to this one was reported by Craig.[29] Cases of primary leptomeningeal cyst in the region of the Sylvian fissures have been reported.[30]

CASE 21.—W. F., a white girl aged 8 years, was referred to the department of pediatrics in July 1936 by Dr. Fred Carpenter, of Newton, Iowa. Four years previously the patient began having attacks of headaches associated with projectile vomiting. There had been progressive diminution of vision, so that she could barely count fingers at 4 feet (1.2 meters). Four weeks before her admission to the hospital her right eye turned inward.

Examination revealed bilateral papilledema, paralysis of the right external rectus muscle and horizontal nystagmus on right lateral gaze. There was a slight droop of the right angle of the mouth. The Babinski tests were accompanied by bilateral plantar extension. The pressure of the spinal fluid was 22 mm. of mercury when the patient was in the prone position. Caloric and Bárány tests as well as audition tests elicited normal responses.

A ventriculogram in the lateral view revealed the third ventricle and enough of the upper segment of the aqueduct to show the characteristic angulation that results from forward displacement due to a tumor of the vermis (fig. 21 *A*). As soon as the cerebellum was exposed, it was obvious that there was a subcortical tumor in the vermis, extending somewhat into the left cerebellar hemisphere. After 20 cc. of yellow fluid was aspirated from the cystic portion, an astrocytoma was removed from the vermis (fig. 21 *B*). The tumor had occupied the entire

29. Craig, W. M.: Chronic Cystic Arachnoiditis, Am. J. Surg. **17**:384-388, 1932.

30. Scherer, Eugene: Ueber Cystenbildung der weichen Hirnhäute im Liquorraum der Sylvischen Furche mit hochgradiger Deformierung des Gehirns, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:787-799, 1935; abstr., Arch. Neurol. & Psychiat. **36**:409 (Aug.) 1936.

vermis, and the roof of the fourth ventricle was removed with it. The histologic appearance of the tumor was that of an astrocytoma, and the yellow fluid contained 120 mg. of cholesterol per hundred cubic centimeters. The patient recovered uneventfully, the disks receded and the pressure of the spinal fluid returned to normal and has remained so to the time of this report (six months). The patient now walks and performs the usual cerebellar tests normally.

CASE 22.—A. Ver D., a white boy aged 14, was referred to the department of pediatrics by Dr. P. M. Henry, of Prairie City, Iowa. For about one month

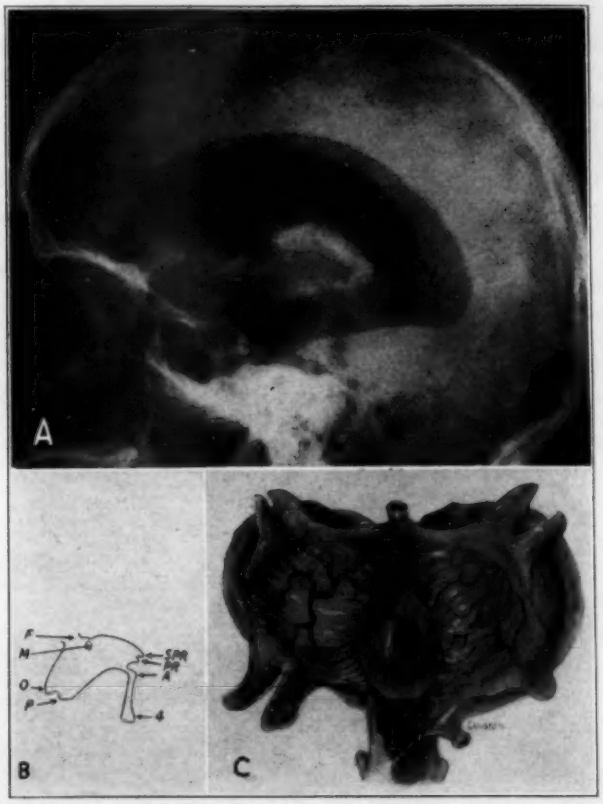

Fig. 20 (case 20).—*A* is a ventriculogram demonstrating a forward displacement of the fourth ventricle and the distal segment of the aqueduct of Sylvius. A sharp angular defect is produced in the upper segment of the aqueduct, which has proved to be constant with tumors in or pressing on the vermis cerebelli. The anatomic analysis of this angulation may be made (fig. 24 *B*). *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *O*, optic recess; *P*, pituitary recess; *SPR*, suprapineal recess; *PR*, pineal recess; *A*, angulation of the aqueduct of Sylvius; *4*, compressed fourth ventricle. *C* is a drawing of the arachnoid (pial?) cyst disclosed at operation.

previous to admission there had been morning vomiting, and the patient complained of dizziness on sudden change of position of his head. He held his chin toward the left shoulder (fig. 22 *B*). His neck was stiff, and his right arm was ataxic.

He limped and had a tendency to fall toward the right. There was bilateral papilledema. The caloric and Bárány tests yielded normal reactions. A ventriculogram showed good visualization of the third ventricle and faint but definite visualization of the upper half of the aqueduct. The latter presented an angular deformity seen in the previous cases of tumor of the vermis (fig. 22 *A*). Cerebellar exploration revealed an astrocytoma. A globular portion 3 cm. in diameter filled

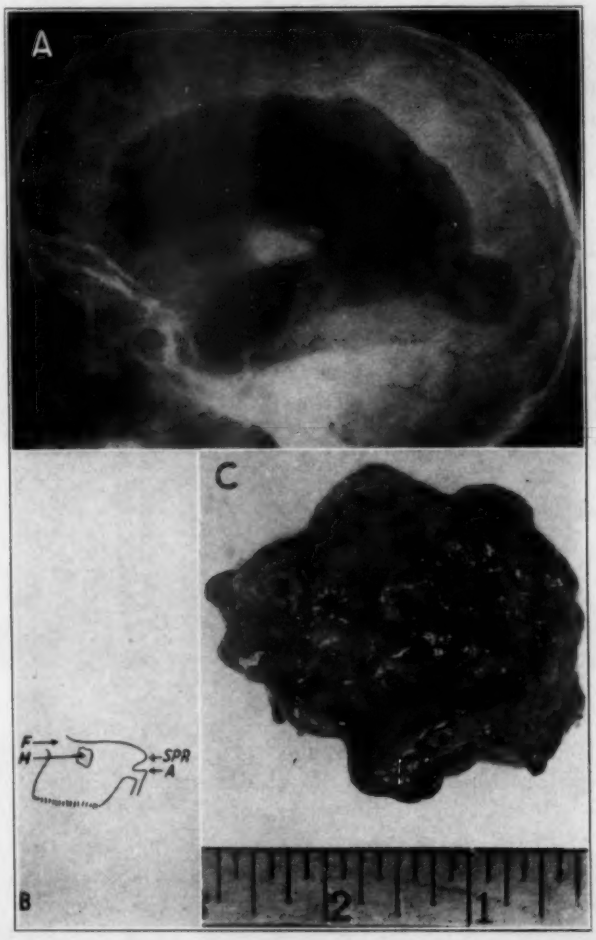

Fig. 21 (case 21).—*A* is a ventriculogram revealing a characteristic angular deformity of the aqueduct due to a tumor of the vermis. *B* is a diagrammatic representation of *A*. *F* indicates the foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *A*, angular deformity of the aqueduct. *C* is a photograph of the unfixed tumor (cystic astrocytoma). The partially collapsed cystic cavity may be seen in the central portion of the mass. The bulk of the tumor completely filled the vermis. The scale is in inches.

the vermis. There was an extension of equal size into the right cerebellar hemisphere, associated with a cyst, from which 25 cc. of clear yellow fluid was taken. The fluid jellied when exposed to the air, and proved to contain 140 mg. of

cholesterol per hundred cubic centimeters. The tumor was extricated, and the patient recovered uneventfully. The circulation of the cerebrospinal fluid was restored to normal dynamics, the disks receded and the vestibular tests again revealed normal reactions.

CASE 23.—L. S., a white man aged 34, was referred to me in August 1935 by Dr. John I. Marker, of Davenport, Iowa. The patient complained of severe and almost continuous right frontal headache and dizziness, which had been present for eight weeks. For six days he had vomited almost everything ingested. On examination the vomiting was observed not to be projectile. The right arm had been amputated, but the left arm was slightly ataxic when the finger to nose test was performed. Examination of the eyegrounds showed only an old choroiditis. A lumbar puncture revealed a cytologically and chemically normal spinal fluid with an initial pressure of 8 mm. of mercury when the patient was in the prone position. The response to the Queckenstedt test was normal in every respect.

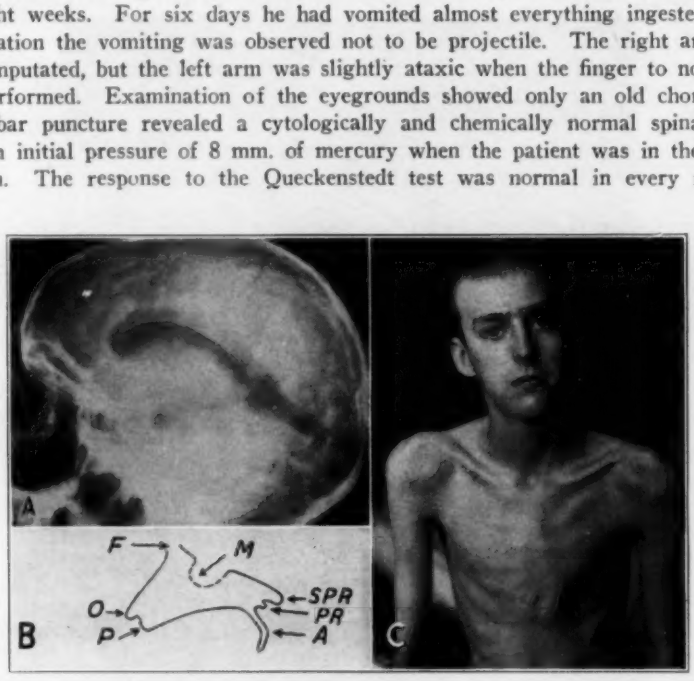

Fig. 22 (case 22).—*A* is a ventriculogram showing angular deformity of the aqueduct of Sylvius. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *O*, optic recess; *P*, pituitary recess; *SPR*, suprapineal recess; *PR*, pineal recess; *A*, angular deformity of the aqueduct due to a cystic astrocytoma of the vermis. *C* is a photograph of the patient showing the habitual posture of the head.

Two subsequent punctures revealed the same normal fluid dynamics. A striking and interesting feature revealed by the examination was a slow pulse rate which varied from 40 to 60 and a slow respiratory rate which varied from 8 to 20. The patient's family physician had noted the bradycardia for some weeks. Any cardiac condition was ruled out by the medical department.

A ventriculogram was made (fig. 23), but before air was injected into the ventricles a manometric reading of pressure in the dependent ventricle in the prone position was 180 mm. of cerebrospinal fluid. Though the anteroposterior view of the ventriculogram showed slightly dilated symmetrical lateral ventricles with some rounding of the angles, the consistently normal pressures were totally out of keeping with the clinical findings. The fourth ventricle had not been revealed, and since visualization of this ventricle was thought to be paramount to a complete

understanding of the situation, air was injected into the spinal theca in addition to the ventricles. The resulting ventriculogram clearly revealed a compression and displacement of the fourth ventricle and lower portion of the aqueduct anteriorly, producing an acute angulation at the junction of the upper third and the lower two thirds of the sylvian aqueduct (fig. 24 *A*). On close inspection of the first ventriculogram, it could be seen that enough of the upper portion of the aqueduct was visible to reveal the angular deformity. Had I been acquainted with this fact at the time, the subsequent combined injection of air would not have been necessary. The diagnosis of a lesion of the vermis was made, and by deep incision of the vermis in the midline a red, highly vascular, cystic, infiltrating tumor was disclosed lying in the anterosuperior aspect of the vermis. After a study of a frozen section it was felt that the tumor was a hemangioblastoma. Some of it was cauterized, and the wound was closed with the hope that some benefit might be derived from irradiation. Hyperthermia developed and the patient died on the fourth postoperative day (fig. 24 *B*).

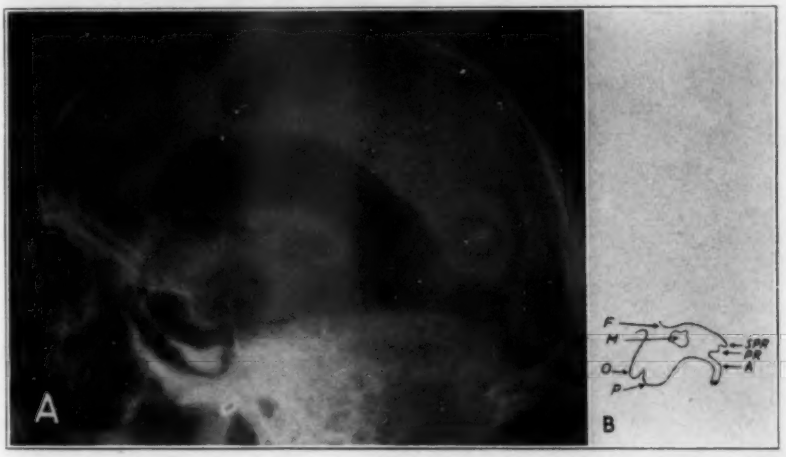

Fig. 23 (case 23).—*A* is a ventriculogram demonstrating the angular deformity of the aqueduct which is pathognomonic of a tumor of the vermis but which was not recognized. This case was my first experience with this ventriculographic entity (fig. 24). *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *O*, optic recess; *P*, pituitary recess; *SPR*, suprapineal recess; *PR*, pineal recess; *A*, angular deformity of the aquduct due to a hemangioblastoma of the vermis.

Case 24.—D. H., a white boy aged 12 years, was referred to me in July 1936 by Dr. J. V. Treynor, of Council Bluffs, Iowa. The patient had had difficulty in walking for three months, and he was bedridden at the time of examination. Incontinence of urine, poor memory and euphoria had been present for three weeks.

Examination revealed bilaterally choked disks and markedly reduced visual acuity. All four extremities were ataxic, and the deep reflexes were hyperactive. When held on his feet, the patient displayed marked retropulsion. His speech was scanning and in monotone. There was a partial palsy of the right side of the face, with deviation of the tongue to the right.

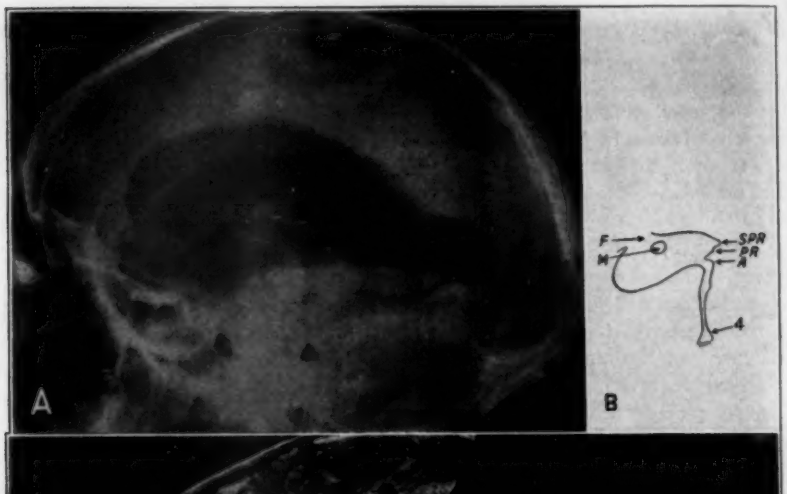

Fig. 24 (case 23).—*A* is a ventriculogram made with combined ventricular and spinal injections of air. There was a more complete filling of the aqueduct and fourth ventricle than previously shown (fig. 23) . The obvious deformity here led to the recognition of the pathognomonic angular deformity in the upper segment of the aqueduct; this has proved to be of diagnostic value in subsequent cases. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *PR*, pineal recess; *A*, angular deformity of the aqueduct; *4*, compressed and anteriorly displaced fourth ventricle. *C* is a photograph of the brain. It may be seen that the angulation of the aqueduct is due to a buckling of the quadrigeminal plate which results from pressure directed anteriorly and superiorly. A portion of the tumor may be seen in the vermis. The greater portion was in the other half of the brain and was a cystic hemangioblastoma. Note the perforation in the septum pellucidum.

The assumption was that of a subtentorial tumor, but a ventriculogram was made. The third ventricle was well visualized, including a dilated proximal segment of the aqueduct of Sylvius sufficient to permit a definite diagnosis of a subtentorial tumor (fig. 25 *A*). The cerebellar tonsils were found herniated to the axis, and a cystic astrocytoma that completely filled the left cerebellar hemisphere and vermis was disclosed; 50 cc. of yellow fluid was removed from the astrocytoma. Several large tumorous nodules, one of which completely filled the vermis, were removed, leaving the fourth ventricle exposed. Cerebrospinal fluid flowed freely through the aqueduct at the termination of the operation. The patient lived two months but made no improvement clinically. A small region in the line of incision became gangrenous from pressure. At this point a fistula developed, which became the source of an intracranial infection.

Necropsy revealed that the tumor had extended high into the mesencephalon, and the aqueduct had been visualized to the point of obstruction. The obstruction was at, or a little above, the point where angulation would have been manifest, and consequently the latter was not present in this case (fig. 25 *B*).

OBSTRUCTION OF THE FORAMEN OF MAGENDIE; ARACHNOIDITIS

Case 25.—D. C., a Negro boy aged 11 years, was referred to the department of pediatrics in September 1935 by Dr. H. C. Bone, of Des Moines, Iowa. Enlargement of the head, vomiting and headache had been present for two years.

The head was markedly enlarged in the anteroposterior direction, and it did not present the spherical enlargement of hydrocephalus. Bilateral papilledema and diminished visual acuity were present. His head leaned a little to the left, and there was evidence of paresis of the left sixth nerve. A ventriculogram revealed greatly dilated lateral ventricles, which were symmetrical and not shifted. The third ventricle was not visualized. Cerebellar exploration revealed marked herniation of the tonsils beneath the atlas. The foramen of Magendie was obstructed by dense adhesions, and when these were broken down cerebrospinal fluid gushed forth from a dilated fourth ventricle. The remainder of the cerebellum proved to be normal. The patient recovered uneventfully, and the pressure of the spinal fluid was restored to normal limits.

I felt that a tumor of the third ventricle or the aqueduct might have been the primary cause of the hydrocephalus and the adhesive arachnoiditis the secondary cause; so ventriculography was repeated twenty-two days after the operation. There was no untoward reaction from this procedure except that the patient remained in a stupor. He could be aroused by conversation, but it was finally necessary to feed him by gavage. Evidence of pulmonary inflammation developed, and he suddenly died of circulatory paralysis eight days later. The last traces of air had been removed from the ventricles four days previous to his death. Permission for necropsy was denied. In spite of the pulmonary complication, this is a case in which the outcome should perhaps be attributed to the repeated injections of air. The second ventriculogram gave clear evidence that the only obstruction had been at the foramen of Megandie (fig. 26). The parents of the patient enlightened us with the fact that his head was elongated at birth; so his pathologic condition may well have been on a congenital basis.

Case 26.—E. G., a white woman aged 30, was referred to the department of neurology by Dr. Frank P. Hanaphy in November 1935. In 1928 the patient had an attack of malaise, anorexia and vomiting which lasted two weeks and which was associated with swollen glands in the neck. For six years thereafter

she had spells of vomiting without nausea, which lasted about a week and which occurred only at Christmas time each year. However, for the past year the patient had had severe morning headaches, often associated with intense vertigo, nausea and projectile vomiting. The vision had become blurred. Aside from marked bilateral papilledema, the neurologic examination gave entirely negative results.

A complete ventriculogram revealed symmetrically dilated lateral ventricles, with an equivalent dilatation of the third and fourth ventricles (fig. 27). An

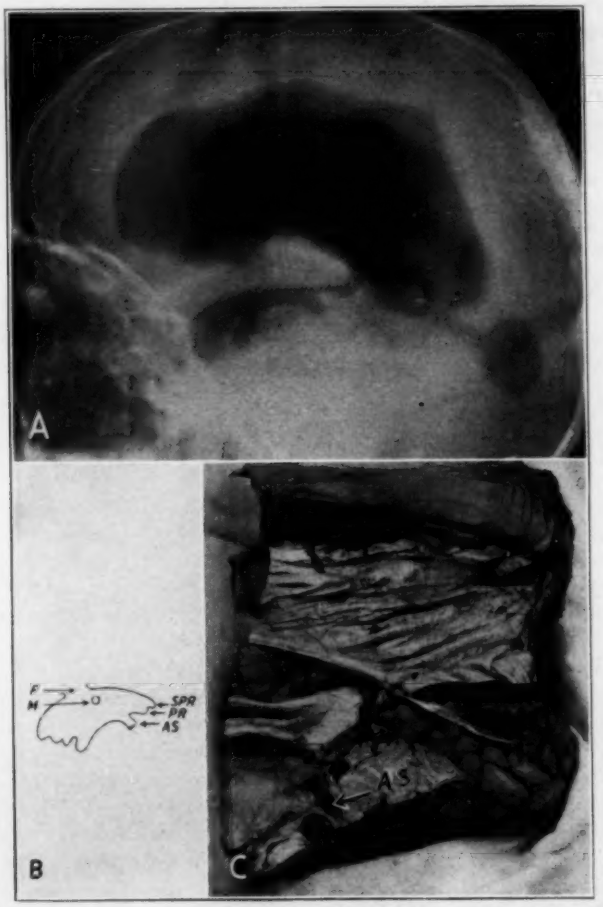

Fig. 25 (case 24).—*A* is a ventriculogram revealing a dilated proximal segment of the aqueduct with visualization to the point of obstruction. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *PR*, pineal recess; *AS*, aqueduct of Sylvius to the point of obstruction. *C* is a photograph of the brain showing the dilated aqueduct indicated by *AS*. The tumor completely obstructed the aqueduct at the plane of section through the brain stem. This precluded the usual angular deformity of the aqueduct.

obstruction of the foramen of Magendie was postulated, and a subtentorial exploration revealed the dura to be slightly adherent to the cerebellar cortex by cobweb-like arachnoid adhesions. The cerebellar tonsils were herniated beneath the atlas,

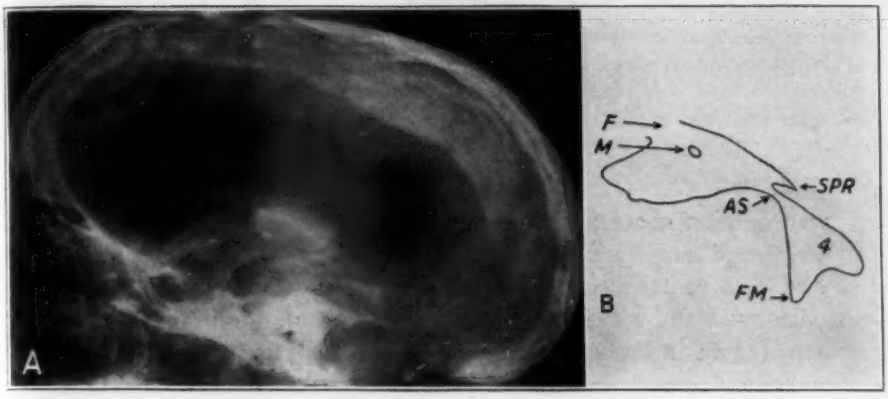

Fig. 26 (case 25).—*A* is a complete ventriculogram demonstrating a dilated third and fourth ventricle to the foramen of Magendie without filling defect. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *M*, massa intermedia; *SPR*, suprapineal recess; *AS*, aqueduct of Sylvius; *4*, dilated fourth ventricle; *FM*, foramen of Magendie.

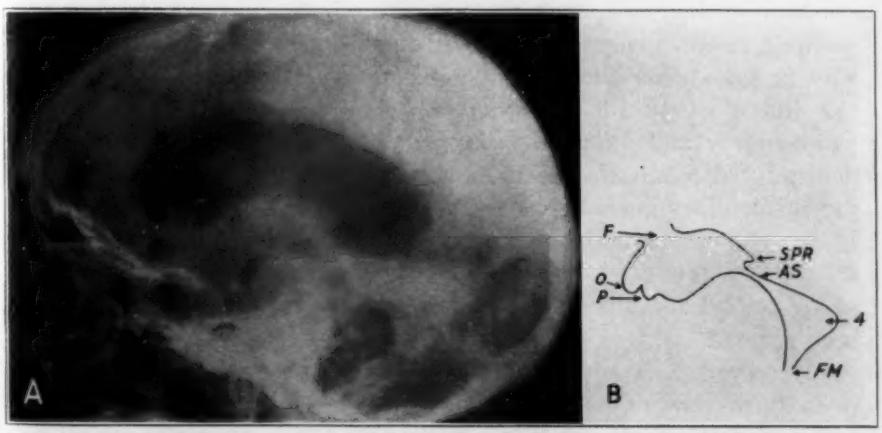

Fig. 27 (case 26).—*A* is a ventriculogram demonstrating a dilated third and fourth ventricle to the foramen of Magendie. *B* is a diagrammatic representation of *A*. *F* indicates foramen of Monro; *O*, optic recess; *P*, pituitary recess; *SPR*, suprapineal recess; *AS*, aqueduct of Sylvius; *4*, dilated fourth ventricle; *FM*, foramen of Magendie, the point of obstruction.

necessitating a removal of its arch. When this was done a gush of fluid came from the spinal arachnoid space. When the tonsils were separated, the foramen of Magendie was found to be obstructed by adhesions except for an opening the size of a tiny pin. The opening was enlarged, bringing a dilated fourth ventricle into view. From a prognostic standpoint, it should be kept in mind that the obstruction may be even distal to the cerebellar cistern, namely, in the basal cisternae. This patient, nevertheless, made a striking recovery, with recession of the papilledema and restoration of the spinal fluid pressure to within normal limits. She has remained in this state of recovery for the past year.

SUMMARY

An opinion concerning the advantage and use of pneumography is given, based largely on my experience. Time and experience have proved that ventriculography is a safe procedure and indispensable to the diagnosis and localization of many tumors of the brain. To obtain the maximum advantage, however, each patient must be treated individually and certain time-tried policies must be strictly observed. It is felt that ventriculography has not yet reached its fullest measure of usefulness, because of illogical and ill founded fear of its application. Its safety and usefulness have been proved, so that now it is only logical to extend its application and incorporate the method of precision whenever it can possibly provide added information of surgical importance. To this end I have given evidence to show that even when the neurologic examination in certain cases has provided data of positive value, a preliminary ventriculogram may be of decided value in planning the optimum method of operative attack. This feeling seems to be contrary to the opinion universally expressed in the literature. It is not in any way proposed that the neurologic examination should not be used to the fullest extent of its resources. However, advances in technical neurosurgery and increasing courage to tackle more serious problems demand that localization be more accurate than neurologic examination can at all times guarantee.

In addition to the more extended application of ventriculography, I have in a few cases found combined ventricular and spinal injection of air helpful and unattended by danger if the intracranial pressure has been relieved.

Moreover, it is advocated that injections of air be complete, particularly in view of localizing tumors in and about the third ventricle, aqueduct and fourth ventricle. Wide variance in operative exposures makes accurate localization here a sine qua non. Cases have been presented to illustrate the possibility and plausibility of obtaining complete ventriculographic information.

CONCLUSIONS

1. Ventriculography has a broader application for the surgeon than is probably yet utilized.

2. The acceptance of symmetrically dilated lateral ventricles as evidence of a subtentorial tumor without an effort by complete injection to prove the status of the third ventricle will lead in some cases to seriously ill chosen exploration. Such errors should no longer be held excusable in the surgeon's mind.

3. A consistent angular deformity of the aqueduct of Sylvius provides ventriculographic evidence of a tumor in or compressing the cerebellar vermis.

ETIOLOGIC FACTORS OF MESENTERIC LYMPHADENITIS

JAY IRELAND, M.D.
CHICAGO

Mesenteric lymphadenitis is an old subject. Bertein and Worms [1] stated that Sydenham in 1723 was the first to describe enlargement of the mesenteric glands in children. Numerous excellent papers have been written on this subject since then describing the pathologic picture, symptoms, diagnosis and treatment. However, the etiology has always been a questionable factor. It was because of this indefinite etiology that this study was undertaken. An attempt has been made to determine the etiologic significance of the various theories previously advocated and also to advance some new ones.

This report is based on a series of twenty-two patients in whom mesenteric lymphadenitis was found at operation at the Children's Memorial Hospital from the years 1931 to 1936 inclusive. Appendectomy was performed on all but two. The appendixes were not removed from these two because intussusception was present in one and intestinal hemorrhages had preceded the operation on the other. The ages of the patients ranged from 2 to 13 years inclusive. There were twelve boys and ten girls. The mesenteric glands varied in size from some that were slightly larger than a pea to a mass the size of a lemon in one case. Intestinal obstruction from the enlarged glands, as reported by Wantoch [2] in two patients, was not observed in this series. Twenty-one of the twenty-two patients recovered, and one died of streptococcic peritonitis due to the rupture of a suppurative gland.

In this report the theories as to the direct agent causing mesenteric adenitis will first be considered, and then the manner of entrance of this agent into the glands will be advanced.

Read before the Chicago Surgical Society, Feb. 5, 1937.

From the Surgical Service of Dr. A. H. Montgomery at the Children's Memorial Hospital.

1. Bertein, P., and Worms, G.: Les adénapathies du mésentère, Gaz. d. hôp. **82**:1291-1295, 1909.

2. Wantoch, H.: Ueber tiefsitzende Duodenalstenose infolge atuberkulöser oder tuberkulöser Lymphdrüsenschwellungen der Mesenterialwurzel, Deutsche Ztschr. f. Chir. **226**:135-139, 1930.

ETIOLOGY

Infections and toxins have probably been advocated as etiologic factors more than any other agents. The idea that an infection from some source is the essential factor is favored by Wilensky and Hahn,[3] Freeman,[4] Brennemann,[5] Short,[6] Struthers,[7] Speese and Klein,[8] Signorelli and Hosen,[9] Coleman [10] and others.

That an actual infection of the glands themselves occurs in some patients is definitely proved. The following case adds further confirmation to this fact:

A boy aged 2 years had abdominal pain for four days and vomiting for two days before admission to the Children's Memorial Hospital. The preoperative diagnosis was acute appendicitis, with rupture and peritonitis. At operation the appendix was found to be normal, but a suppurative peritonitis was present. Appendectomy was performed, and the patient died on the same day. Necropsy disclosed a ruptured mesenteric lymph gland with generalized peritonitis, as shown in the illustration. Necrotic portions of the gland yielded Streptococcus haemolyticus on culture. Microscopic sections from the colon showed a well preserved mucosa which contained perhaps a slightly increased number of cells in its loose stroma. A few lymphoid follicles seen in this section showed active germination. There was some edema of the submucosa. Many mononuclear wandering cells of various forms and many polymorphonuclears were found in

3. Wilensky, A. O., and Hahn, L. J.: Mesenteric Lymphadenitis, Ann. Surg. **83**:812-826 (June) 1926. Wilensky, A. O.: Mesenteric Lymphadenitis, M. Rec. **98**:770-772 (Nov. 6) 1920.

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5. Brennemann, J.: The Abdominal Pain of Throat Infections, Am. J. Dis. Child. **22**:493-499 (Nov.) 1921; The Clinical Significance of Abdominal Pain in Children, Surg., Gynec. & Obst. **34**:344-350 (March) 1922; Throat Infections in Children, Arch. Pediat. **42**:145-168 (March) 1925; "The Abdominal Pain of Throat Infections in Children," and Appendicitis, J. A. M. A. **89**:2183-2186 (Dec. 24) 1927.

6. Short, A. R.: Symptoms Due to Mesenteric Lymphadenitis, Lancet **2**: 909-912 (Nov. 3) 1928.

7. Struthers, J. W.: Mesenteric Lymphadenitis Simulating Appendicitis, Edinburgh M. J. **27**:22-26 (July) 1921.

8. Speese, J., and Klein, T.: Acute Mesenteric Lymphadenitis Associated with Chronic Appendicitis, S. Clin. North America **4**:261-263 (Feb.) 1924. Speese, J.: Mesenteric Adenitis, Pennsylvania M. J. **32**:225-228 (Jan.) 1929.

9. Signorelli, J., and Hosen, H.: Chronic Abdominal Discomfort in Children, New Orleans M. & S. J. **88**:353-357 (Dec.) 1935.

10. Coleman, E. P.: (*a*) Acute Mesenteric Lymphadenitis, West. J. Surg. **43**:193-198 (April) 1935; (*b*) The Diagnosis of Mesenteric Lymphadenitis, Illinois M. J. **68**:408-413 (Nov.) 1935.

the outer muscular layer. In one area there was a large portion of autolyzed mucosa. Similar changes were found in the small section of the ileum. A Gram stain failed to reveal organisms in the intestinal wall.

Similar cases of purulent abscess formation from necrotic mesenteric lymph glands have been described previously by Nyström,[11] Pólya and von Navratil,[12] Borchard,[13] Doyen,[14] Johnsson-Breuer [15] Wilensky and Hahn,[3] Etchegorry [16] and Calvanico.[17]

Head [18] reported a case of tuberculous mesenteric lymphadenitis in which secondary infection and rupture occurred. He found two similar cases reported in the literature.

Attempts to find organisms in the glands removed at operation have usually been unsuccessful. Wilensky and Hahn [3] found a gram-negative bacillus in the abdominal fluid of one patient and recovered Str. haemolyticus from a suppurative gland of another. Marshall [19] cultured the glands of an unstated number of his forty-eight patients and found B. coli in two instances. Goldberg and Nathanson [20] found Str. haemolyticus in the glands of one of eight patients. Heusser [21] examined the glands of twenty-five of his patients and found B. coli in only two. In the present series, Str. haemolyticus was cultured from a lymph gland of the patient who died.

Strömbeck [22] found mesenteric lymphadenitis associated with paratyphoid infection in a patient on whom he operated.

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11. Nyström, G.: Studier öfver resultaten af behandling för appendicit vid akademiska sjukhuset i Uppsala (kirurgi), Nord. med. Ark. (supp.) **7**:1-258, 1907.

12. Pólya, E., and von Navratil, D.: Untersuchungen über die Lymphbahnen des Wurmfortsatzes und des Magens, Deutsche Ztschr. f. Chir. **69**:421-456, 1903.

13. Borchard, A.: Die primäre Lymphangitis des Wurmfortsatzes, Deutsche med. Wchnschr. **54**:1074-1075 (June 29) 1928.

14. Doyen, cited by Strömbeck.[22]

15. Johnsson-Breuer, cited by Strömbeck.[22]

16. Etchegorry, P. A.: Linfadenitis mesentérica supurada, Semana méd. **1**: 990-993 (April 21) 1927.

17. Calvanico, R.: Le modificazioni dell'apparato linfo- adenoideo locale dell'appendicite, Policlinico (sez. chir.) **34**:253-275 (June) 1927.

18. Head, J. R.: Tuberculosis of the Mesenteric Lymph-Glands, Ann. Surg. **83**:622-633 (May) 1926.

19. Marshall, C. J.: Simple Ileo-Caecal Lymphadenitis, Brit. M. J. **1**:631-632 (April 14) 1928.

20. Goldberg, S. L., and Nathanson, I. T.: Acute Mesenteric Lymphadenitis: Clinical Syndrome in Children Simulating Appendicitis, Am. J. Surg. **25**:35-40 (July) 1934.

21. Heusser, H.: Die Schwellung der mesenterialen Lymphdrüsen, Beitr. z. klin. Chir. **130**:85-98, 1923.

22. Strömbeck, J. P.: Mesenteric Lymph-Adenitis: A Clinical Study, Acta chir. Scandinav. (supp. 20) **70**:1-254, 1932.

It has been suggested that possibly mesenteric lymphadenitis is due to the same agent which produces lymphogranuloma venereum. Cole [23] stated that this disease may cause generalized lymphadenopathy, and the inoculation of mice by von Haam and D'Aunoy [24] with the virus of lymphogranuloma venereum was followed by evidence of a generalized infection. One might hypothecate that a similar infection could occur in man. Furthermore, Kondo,[25] Reichle and Connor [26] and Kornblith [27] reported cases of lymphogranuloma venereum in which involvement of the retroperitoneal lymph nodes was found at necropsy. David and Loring [28] emphasized the frequency of extragenital occurrence. Thompson [29] stated that a primary sore was present in about 50 per cent of patients with lymphogranuloma venereum, but there was no history or evidence of a primary lesion in any of the patients in the present series.

Frei tests were made on twelve of the patients from seven days to four years and two hundred and eighty-three days after appendectomy. This was considered ample time for the test to become positive, since Cole [23] stated that it becomes positive from four to twenty-one days after adenitis begins. He also pointed out that after an attack of lymphogranuloma venereum the Frei test probably remains positive for life. In the present series all of the twelve patients on whom Frei tests were made had negative reactions. Therapy with lymphogranuloma venereum antigen, as employed by Bloom,[30] or solganal (the disodium salt of 4-sulfomethylamino-2-auromercaptobenzene-1-sulfonic acid), as employed by Gohrbandt,[31] was not used to make a diagnosis.

For many years tuberculosis was considered the principal and probably the only cause of mesenteric lymphadenitis by some of the older

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23. Cole, H. N.: Lymphogranuloma Inguinale, the Fourth Venereal Disease, J. A. M. A. **101**:1069-1076 (Sept. 30) 1933.

24. von Haam, E., and D'Aunoy, R.: Infectivity of Spinal Fluid in Lymphogranuloma Inguinale, J. A. M. A. **106**:1642-1643 (May 9) 1936.

25. Kondo, S.: Ueber akute Peritonitis, durch Lymphogranuloma inguinale-Virus verursacht, Arch. f. klin. Chir. **184**:249-257 (Dec.) 1935.

26. Reichle, H. S., and Connor, W. H.: Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **32**:196-203 (Aug.) 1935.

27. Kornblith, B. A.: Observations on Lymphogranuloma Venereum, Surg., Gynec. & Obst. **63**:99-109 (July) 1936.

28. David, V. C., and Loring, M.: Extragenital Lesions of Lymphogranuloma Inguinale, J. A. M. A. **106**:1875-1879 (May 30) 1936.

29. Thompson, R. M.: Lymphopathia Venereum, J. A. M. A. **106**:1869-1875 (May 30) 1936.

30. Bloom, D.: Strictures of the Rectum Due to Lymphogranuloma Inguinale, Surg., Gynec. & Obst. **58**:827-840 (May) 1934.

31. Gohrbandt, E.: Miterkrankung des Rectum und des Urogenitalsystems bei Lymphogranulomatosis inguinalis, Arch. f. klin. Chir. **177**:611-617 (Oct.) 1933.

writers, such as Struthers,[7] McFadden [32] and others. Bell [33] stated that the condition should be considered as tuberculous until proved otherwise. McFadden [32] thought that the tuberculosis was probably bovine in type. While there is no doubt that there are cases of mesenteric lymphadenitis due to tuberculosis, they represent a small minority at the present time.

Strömbeck [22] removed the glands of fourteen patients, and those of four were proved to be negative for tuberculosis on inoculation of guinea-pigs. Heusser,[21] by means of cultures, the sodium hypochlorite test and inoculation of guinea pigs, apparently proved the absence of tuberculosis in his forty patients. Freeman [4] removed glands from fifty patients, and those of forty-three proved to be negative for tuberculosis. In ten cases inoculation of guinea pigs were made, and evidence of tuberculosis was found in only four. Strömbeck [22] made a roentgenographic examination of the abdomen for calcified lymph glands in thirty patients from twenty months to nine years after operation, with negative findings for tuberculosis. In 85 per cent of his forty patients he ruled out tuberculosis with as great a degree of certainty as clinical examination admitted.

A tuberculin test was made on eight patients in the present series, and a negative reaction was uniformly found.

Lewis [34] suggested that Bacillus melitensis, the causative organism of undulant fever, might be an etiologic factor. However, Davison [35] stated that in undulant fever the white blood count is reduced or is normal. In twenty-one of the twenty-two patients in the present series, the leukocyte count ranged from 4,600 to 26,500 per cubic millimeter of blood. In seventeen, the count ranged from 10,200 to 26,000, which was considered above normal; in three, it ranged from 7,500 to 10,000, which was considered normal, and in one, it was 4,600, which was considered indicative of leukopenia. Such blood pictures militate against the conception that B. melitensis was the causative organism in all cases.

In addition, cultures of the urine of four patients and of the stools of two were made for B. melitensis, and all were negative. Agglutination tests with B. melitensis and the patient's blood were also made on two patients, and the results were the same. From these observations it would seem evident that B. melitensis is hardly worth considering as a causative agent.

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32. McFadden, G. D. F.: Mesenteric Lymphadenitis and Its Clinical Manifestations, with Special Reference to Its Differential Diagnosis from Appendicitis, Brit. M. J. **2**:1174-1177 (Dec. 24) 1927.

33. Bell, L. P.: Mesenteric Lymphadenitis Simulating an Acute Abdominal Condition, Surg., Gynec. & Obst. **45**:465-473 (Oct.) 1927.

34. Lewis, Dean, cited by Freeman.[4b]

35. Davison, W. C.: Brucellosis, Bull. Chicago Med. Soc. **38**:552 (March 21) 1936.

Heusser,[21] Brüning,[36] Guleke [37] and Wagner [38] considered intestinal parasites as causative factors. Parasites were found in the appendix in only one patient of the present series.

White and Collins [39] suggested that poliomyelitis might be the causative agent but presented no real proof to substantiate their belief.

The idea that a toxin is the cause of enlargement of the glands in many patients has not been disproved. Bell [33] expressed the belief that bacterial toxins were the cause. Coleman [10] thought that a streptococcus toxin was probably the causative agent. The outstanding fact that attempts to find the organism in the glands removed at operation have usually been unsuccessful indicates that a toxin may possibly be the underlying factor in many cases. However, it has been definitely excluded in some patients in whom organisms have been found.

PORTAL OF ENTRY

Conceptions of the portal of entrance of the causative agent into the glands have differed.

Of the various avenues which have been suggested, the appendix has probably received the most attention. It was believed to be the most probable route by Brown,[40] Pribam,[41] Coleman,[10] Royster,[42] Short,[6] Lamson,[43] Freeman,[4] Speese,[8] Segar and Rosenak [44] and others. Strömbeck [22] found microscopic changes in the appendix in twenty-seven of his thirty-nine patients with mesenteric lymphadenitis. However, Goldberg and Nathanson [20] found histopathologic changes, other than slight lymphoid hyperplasia, in only two appendixes in their sixteen

36. Brüning, F.: Ueber Mesenteriitis, Mesenteriolitis und Mesocolitis, Arch. f. klin. Chir. **145**:257-267 (March) 1927.

37. Guleke, N.: Die Hyperplasie der Mesenterial-Lymphdrüsen, Arch. f. klin. Chir. **133**:517-532, 1924.

38. Wagner, J.: Acute Mesenteric Lymphadenitis Following Trauma and Simulating Acute Appendicitis, Internat. J. Surg. **38**:113-114, 1925.

39. White, C. S., and Collins, J. L.: Acute Mesenteric Adenitis, J. A. M. A. **107**:1023-1025 (Sept. 26) 1936.

40. Brown, H. P.: Acute Mesenteric Adenitis Simulating Appendicitis, S. Clin. North America **9**:1195-1196 (Oct.) 1929.

41. Pribam, B. O.: Ueber Lymphangitis mesenterialis, Arch. f. klin. Chir. **140**:589-600, 1926; Die Lymphangitis mesenterialis als abdominelle Herdinfektion, Substrat der peritonealen Adhäsionen und Bindeglied zwischen den sogenannten zweiten Krankheiten, ibid. **160**:362-389, 1930; Das Krankheitsbild der Lymphangitis mesenterialis und peritonealis, Med. Klin. **27**:871-875 (June 12); 911-913 (June 19) 1931.

42. Royster, H. A., cited by Freeman.[4b]

43. Lamson, O. F.: Mesenteric Lymphadenitis and Acute Appendicitis, S. Clin. North America **11**:1061-1063 (Oct.) 1931.

44. Segar, L. H., and Rosenak, B. D.: Non-Tuberculous Mesenteric Lymphadenitis in Childhood, Am. J. Digest. Dis. & Nutrition **2**:356-360 (Aug.) 1935.

proved cases of mesenteric lymphadenitis. Quenu [45] and Marchant [46] conciliated these observations by stating that there was an alteration in the appendixes in some of these patients but not in others.

The appendixes of nineteen of the patients in the present series were examined microscopically, and only eight showed any evidence of pathologic change. In one appendix there was hypertrophy of the lymphoid follicles; four showed acute inflammation and one subacute inflammation; one contained Oxyuris vermicularis and showed focal infiltration with polymorphonuclear leukocytes and eosinophils, and in one there was focal ulceration confined to the submucosa.

Royster [42] thought that the cause in some of these cases of mesenteric lymphadenitis was a lymphatic block around the appendix and that the removal of the appendix mechanically released the block. Freeman [4] pointed out that involvement of the lymph gland in mesenteric lymphadenitis is usually quite diffuse throughout the abdomen and that the lymphatic drainage of the appendix is local. It should be emphasized that the appendix is a part of the large bowel and that it is a well known fact that the mesenteric lymph glands are frequently not enlarged in cases of acute or of chronic appendicitis.

It may be possible that a kinking, twisting or obliteration of the lumen of the appendix may be a factor in some patients. However, an anatomic condition of this character was found in the appendix in only two patients in the present series and consisted of a kinking of the organ.

Brown,[40] Royster [42] and others, who believed that the appendix was the essential causative factor in mesenteric lymphadenitis, advocated appendectomy. Royster [42] reported that following this treatment none of his patients had any further trouble.

Apparently, however, appendectomy does not cure all of these patients, for Marshall [19] followed up an unstated number of his twenty-six patients after appendectomy and found that four of them had attacks postoperatively. This observation is further confirmed by Schnitzler's [47] experience. Appendectomy was performed on his patient, and eight years later the patient was operated on by him under the mistaken idea that appendectomy had not been performed previously. Simple mesenteric lymphadenitis was found at this second laparotomy, and, furthermore, the patient subsequently continued to have similar attacks.

Similarly, in the present series, a boy aged 7 years, who presented the clinical picture of acute appendicitis, underwent an appendectomy on May 1, 1933. He was free from symptoms the following two months,

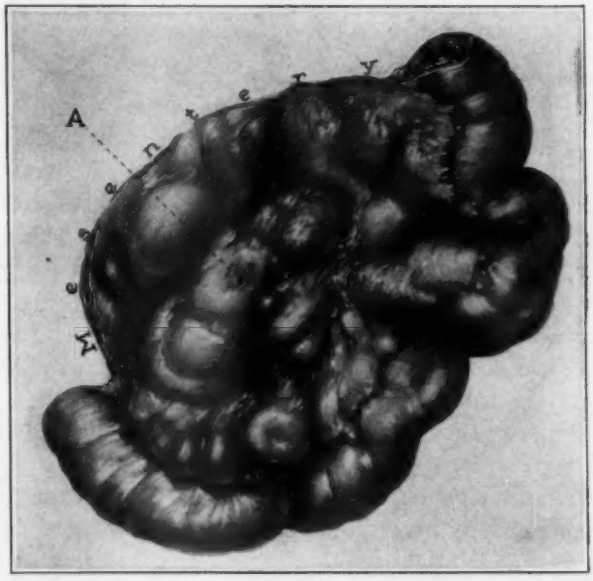
45. Quenu, cited by Bertein and Worms.[1]

46. Marchant, G.: Adénite dans l'appendicite, Bull. et mém. Soc. de chir. de Paris **26**:77-81, 1900.

47. Schnitzler, H.: Lymphangitis et Lymphadenitis mesenterialis, Wien. klin. Wchnschr. **46**:134-137 (Feb. 3) 1933.

and then another attack of pain in the abdomen, fever and nausea developed. These symptoms continued intermittently, and nine months after operation another laparotomy was performed, at which a mass of mesenteric lymph glands 3 by 5 cm. was found in the center of the upper part of the mesentery. Other enlarged glands were also found scattered throughout the mesentery.

Strömbeck,[22] who examined forty patients with mesenteric lymphadenitis, aged 1 to 40 years, on an average of three and nine-tenths years after simple appendectomy, found that thirty-three (87 per cent) were free from symptoms. However, five had the same abdominal



Necropsy specimen showing numerous enlarged mesenteric lymph glands and a section of the small bowel. The perforation (*A*) of a gland is shown.

symptoms postoperatively as preoperatively. One died from diphtheria and one from ileus.

Many observers, such as Wilensky and Hahn,[3] Carson [48] and Goldberg and Nathanson,[20] expressed the belief that the appendix has no clinical relation to mesenteric lymphadenitis. All of these authors had extensive experience with this disease.

Of the twenty-two patients in the present series, twenty were traced and reexamined. These final examinations were made from sixty days to four years and two hundred and eighty-five days after appendectomy. Sixteen of them had had no kind of abdominal distress simulating

48. Carson, H. W., cited by Freeman.[4b]

another attack of mesenteric lymphadenitis since operation, but four were found to have attacks much like those present before operation.

It would seem, however, that the weight of evidence is against those who believe that an infection from the appendix can be excluded as a causative factor in mesenteric lymphadenitis. The percentage of recoveries after appendectomy seems too high to be a mere coincidence. Since most of the patients are free from symptoms after removal of the appendix, appendectomy is apparently indicated when simple mesenteric lymphadenitis is present and no cause other than the appendix is found for its presence. It may be, as suggested by Schnitzler,[47] that an infection in the appendix and one in the mesenteric lymph glands do not occur pari passu and that the lesion of the appendix has healed by the time the glands become enlarged.

In regard to another portal of infection, Brennemann [5] suggested that bacteria may be transmitted from the throat by the blood stream or may be swallowed and produce localized inflammatory lesions in the intestines with secondary involvement of the lymph glands. Cultures of material from the throat by Goldberg and Nathanson [20] invariably showed Str. haemolyticus and in addition some showed Staphylococcus haemolyticus. They thought the mode of infection to be hematogenous. In the present series of twenty-two patients, there were fifteen (68 per cent) who presented evidence of infection of the upper respiratory tract at the time of operation or just preceding it. It is reasonable to suppose that a higher percentage would have been found if such evidence had been carefully looked for in every instance. The incidence here recorded is based on the routine hospital records, and it is quite probable that a critical evaluation as to the presence of an infection of the throat at the time of or immediately preceding operation, not always a simple matter at best, was not made in all cases. Coleman [10] stated that in his patients the infection seemed to come from the respiratory or the intestinal tract. Ninety per cent of his patients had enlarged cervical glands.

Guleke,[37] in common with most observers, expressed the belief that the etiologic agent came from the bowel. Various factors which might favor the passage of bacteria or their toxins through the wall of the bowel have been suggested. Distention, catarrhal inflammation, abrasions of the mucous membrane and lowered resistance of the surface epithelium of the bowel were thought to be important in the production of mesenteric lymphadenitis according to Bell,[33] Pribam,[41] Freeman [4] and Signorelli and Hosen.[9]

Marshall [19] resected a portion of the cecum with the appendix of one patient and found no catarrh of the cecum microscopically. Stained sections were made of the wall of the bowel for bacteria in the fatal case of the series which forms the basis of this report, but no organisms were found.

Strömbeck [22] thought incompetence of the ileocecal valve with autoinfection of the ileum was probable.

Pribam [41] and Bell [33] thought stasis of the bowel a factor.

Crohn, Ginzburg and Oppenheimer [49] reported one case due to regional ileitis.

Trauma was considered a factor by Wagner [38] in one case which he reported.

Allergy seemed certainly to be the causative factor in one patient of the present series who had attacks of abdominal pain after appendectomy similar to those before operation. Epinephrine hydrochloride given hypodermically during the paroxysms of pain gave relief. Eggs, pineapples and blueberries were removed from the diet, and the attacks ceased immediately and had not recurred at the last examination, eleven months after these offending foods were eliminated.

Careful studies were made of the two other patients who had attacks after appendectomy, but the cause was not found.

From a review of the cases of mesenteric lymphadenitis seen at the Children's Memorial Hospital and of those reported in the literature, it seems clear that there is no one etiologic factor that is responsible for the condition, as was pointed out by Strömbeck [22] and by Hess.[50]

SUMMARY

Laparotomy was performed on twenty-two patients who had simple nontuberculous mesenteric lymphadenitis.

One patient died with an abscess formation due to Str. haemolyticus and rupture of a mesenteric gland.

Twenty patients were examined from sixty days to four years and two hundred and eighty-five days after appendectomy, and seventeen were free from symptoms.

Frei tests were performed on twelve patients, and all were negative.

Tuberculin tests were performed on eight patients, and all were negative.

Cultures of the urine of four patients and of the stools of two patients and agglutination tests performed on two patients for B. melitensis all gave negative results.

The appendix should be removed when no other cause is found for the enlarged mesenteric glands.

Allergy was found to be a cause of abdominal distress in one patient.

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49. Crohn, B. B.; Ginzburg, L., and Oppenheimer, G.: Regional Ileitis: Pathologic and Clinical Entity, J. A. M. A. **99**:1323-1328 (Oct. 15) 1932.

50. Hess, J. H., in discussion on Coleman,[10b] p. 412.

CONCLUSION

The opinion regarding the etiology of mesenteric lymphadenitis are numerous and varied. There is one group of investigators who believe that it is due to tuberculosis, but there is also a large group who found no evidence of tuberculosis by test or by culture. It seems that there is no definite evidence either in the literature or from tests made on the patients in the present series that the virus of lymphogranuloma venereum or B. melitensis plays any part in the production of this condition. It is concluded that the infection in some patients does and in some does not appear to originate from the appendix. Many observers believe that these infections come from pyogenic infection in the throat which enters the glands by the blood or through the wall of the bowel. It would appear from the observations reported and from a careful review of the literature that not one but several factor are capable of producing mesenteric lymphadenitis.

5412 North Clark Street.

NOTE.—Since we made this report there have been added two interesting cases of mesenteric lymphadenitis. In one a ruptured mesenteric gland was found at autopsy, and in another, regional ileitis.

TERATOMA OF THE PINEAL BODY

CLASSIFICATION OF THE EMBRYONAL TUMORS OF THE PINEAL BODY; REPORT OF A CASE OF TERATOMA OF THE PINEAL BODY PRESENTING FORMED TEETH

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Teratoma of the pineal body is surprisingly rare considering the many possibilities for that type of tumor formation inherent in the body. The literature contains reports of only thirteen cases of proved teratoma, four cases of teratoid tumor and one case of chorionepithelioma of the pineal body. These constitute approximately 10 per cent of all the reported tumors of the pineal body. To this series there is here added a new case, which is unique in that it presents for the first time all stages in the development of adult teeth.

DEFINITION AND CLASSIFICATION OF EMBRYONAL NEOPLASMS [1]

Considerable confusion exists in the literature on the subject of embryonal and mixed tumors of the pineal body, largely because of the lack of uniformity in the terminology applied. At the very beginning of this paper, therefore, definition and classification of the terms which we shall use will be made. This classification follows in general the works of Bostroem and of Brock and Klenke, with certain modifications of our own.

An embryonal neoplasm is a tumor derived from a primitive cell group which has become isolated from the normal growth pattern during embryonal life and has retained and exercised, in whole or in part, the

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This case report was presented in abstract at the annual meeting of the American Association of Pathologists and Bacteriologists, March 1934.

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1. Embryonal neoplasms approximate 1 per cent of all the intracranial tumors. Dr. Cushing's series of 1,936 intracranial tumors included 11 epidermoid tumors, 3 teratoid tumors and 4 teratomas. In a series of 450 tumors studied at the New York Neurological Institute there were 4 epidermoid tumors, 2 teratoid tumors and no teratomas.

powers of further differentiation which were inherent in the original cells at the time of their separation.

The epidermoid tumor is an embryonal neoplasm composed of tissues derived entirely from ectodermal elements. Certain of the craniopharyngiomas, e. g., the cholesteatoma and the simple adamantinoma, properly may be considered to fall within this classification. Although the epidermoid tumor is the most frequent form of intracranial embryonal tumor, it is interesting that not a single epidermoid tumor has been reported as arising from the pineal body. The significance of this observation will be discussed later.

The teratoid tumor is an embryonal growth composed of tissues derived from both ectodermal and mesodermal elements. Certain of the more complex craniopharyngiomas might be considered to fall within this classification. The common clinical "dermoid" tumor, usually made up of a fibrous sac bearing hair and sebaceous material, is in reality a teratoid tumor of limited character. It is our opinion that the four cases reported in the literature as dermoid tumors of the pineal body should be classified as teratoid tumors and we are so referring to them hereafter in this paper.

The teratoma is an embryonal tumor composed of tissues derived from all three primitive layers. A tumor of this type is comparatively infrequent within the cranium. Teratoma of the pineal gland has been reported and the diagnosis proved in only thirteen instances prior to the case reported here.

A chorionepithelioma is an embryonal neoplasm in that it is composed of primitive cells derived directly from the fetal epiblast. The usual source of a chorionepithelioma is the fetal epiblast of the retained placenta; nevertheless, such a tumor is occasionally encountered as a spontaneous evolution from the germinal epithelium of the ovary or the testis. One instance of chorionepithelioma primary in the pineal body has been reported by Askanazy. This tumor must be considered as an embryonal neoplasm that had taken origin from a primitive cell group comparable to the germinal epithelium of the testis and that had differentiated up to the level of the fetal epiblast. However, as the tumor presents no evolved ectodermal or mesenchymal tissues, it cannot be classified as an epidermoid or teratoid tumor or as a teratoma and is therefore given an individual subgrouping with the embryonal neoplasms.

MIXED TUMORS

In addition to the true embryonal neoplasms listed, mention should be made of the "mixed" or "compound tumor" of the pineal body, which is made up of two or more differentiated neoplastic elements. Reports

of ten such cases of mixed tumor of the pineal body have at various times appeared in the literature under the heading teratoma. This we believe to be an error, likely to be misleading, and therefore shall discuss this type of tumor formation and list it separately, in an attempt to clarify the situation.

A tumor may arise in the fully formed pineal body, as in any other complex organ, from one or more of the constituent cellular elements. The mixed tumor falls outside the category of the embryonal neoplasm because the cells from which it originates are not necessarily primitive but rather groups of well differentiated cells that have broken into an unregulated growth, and which, in the course of the tumor growth, undergo no further structural evolution. The parenchymal cell of the pineal body may give rise to the pineal adenoma, better known as a "pinealoma," and the neuroglia of the pineal body to the gliablastoma, or "spongioblastoma multiforme;" the occasional ganglionic elements may form a ganglioneuroma and the fibrovascular element a sarcoma or a hemangioma. Cysts, though at times classed among the new growths, are better considered as the vestigial remains of the original pineal recess. The formation of cartilage as a metaplastic phenomenon is a common finding in sarcoma and does not merit special attention in this discussion.

Admixture of these various tumor elements will form such neoplasms as "ganglioglianeuroma" (Schmincke), "neuroglioma-ependymale" (Pappenheimer) and others. These mixed tumors have been referred to by Marburg as "compound tumors" of the pineal body. They simulate the mixed tumor of the parotid gland in their pathologic entity.

ORIGIN OF EMBRYONAL TUMORS WITHIN THE CRANIUM

Embryonal neoplasms arising within the cranium originate principally from remains of the craniopharyngeal (craniobuccal) invagination, from anomalous cell rests or inclusions occurring during the invagination of the dorsal medullary groove and from the pineal body.

The tumors arising from the ventral and dorsal invaginations have much in common. Primarily they are relatively simple in comparison with the more complex tumors of the pineal body. In general, these tumors are structurally identified with the epithelium from which they sprang or with elements that were immediately derived from that epithelium. A tumor taking origin from the craniobuccal pouch, for instance, exhibits the type of epithelium found in the mouth and pharynx—squamous epithelium and adamantinomatous structure; a tumor which is derived from the dorsal ectoderm exhibits squamous epithelium, sebaceous glands and hair. It would appear from a study of such tumors that

TABLE 1.—*Data on Embryonal Tumors of the Pineal Body Reported in the Literature*

Case No.	Date	Author	Sex	Age, Yr.	Clinical Data	Duration of Illness	Location, Type and Size	Pathologic Picture: Ectoderm	Pathologic Picture: Mesoderm	Pathologic Picture: Endoderm	Comment
							TERATOMAS *				
1	1875	Weigert	M	14	Patient admitted in comatose state; emaciated	.....	3d ventricle; cystic; 1⅜×1½ inches	Squamous epithelium, cornified; hair; hair follicles; sebaceous glands; nests of pineal tissue; nonmedullated nerve fibers	Connective tissue; fat; cartilage; smooth muscle	Columnar epithelium with papillary formation	
2	1889	Gauderer	M	12	Frontal headaches; patient lethargic in thought and action; well nourished; late signs of local and general compression	.....	3d ventricle; cystic; 3.5×2.5 cm.	Squamous epithelium; hair; sebaceous glands	Connective tissue; hyaline cartilage; fat; bone; osteoid tissue; smooth muscle	Columnar epithelium, mucosal type	
3	1896	Gutzeit	M	8	Frontal headaches; genital precocity; lethargy; late signs of local and general compression	8 mo.	3d ventricle; cystic; 4×3.25 cm.	Epidermoid epithelium; hair; sebaceous glands	Connective tissue; cartilage; fat; smooth muscle	Columnar epithelium	
4	1900	Neumann	M	27	Midfrontal headaches; lethargy; signs of local and general compression	7 wk.	3d ventricle; cystic; 4×3×2.5 cm.	Squamous epithelium, cornified; cholesterol-filled cysts; epidermoid carcinoma; pineal tissue	Connective tissue—sarcoma (?); hyaline cartilage; fat; lymphoid tissue; blood vessels—hemangioma; smooth and striped muscle	Columnar epithelium with cuticle and gland formations	
5	1900	Frankl-Hochwart	M	5½	Overgrowth; macrogenitalia; adiposity; hypertrichosis; maturity of voice and mental status; late signs of local and general compression; congenital defects—bronchial fissure, nevi and hemangiomas	2½ yr.	3d ventricle; cystic; 5×2.5×2.9 cm.	Squamous epithelium, cornified; pineal tissue	Connective tissue—sarcoma (?); hyaline embryonal cartilage; osteoid tissue; round cell infiltration	Columnar epithelium with goblet cells and gland formation	Congenital familial defects; tumor of the pineal body diagnosed before death on basis of macrogenitosomia praecox
6	1913	Hijmans, van den Bergh and van Hasselt	M	8	Overgrowth; macrogenitalia; hypertrichosis; maturity of voice and mental status; polyuria; polydipsia	.....	3d ventricle; cystic	Squamous epithelium, cornified; hair; sebaceous glands; pineal tissue; ganglion cells; nerve fibers; epithelioid cells of indifferent character in nests and syncytial masses	Connective tissue; bone; cartilage; lymphoid tissue	Columnar epithelium	Epithelioid nests suggest chorioepitheliomatous structure; teratoma of the pineal body diagnosed before death on the basis of macrogenitosomia praecox
7	1913	Hueter	M	19	Headache; signs of general compression	.....	3d ventricle; size of pigeon's egg	Squamous epithelium; pineal tissue	Connective tissue; smooth muscle	Columnar epithelium with gland formation of the gastrointestinal type	No histopathologic report with original presentation, but complete picture is presented and illustrated by Berblinger
8	1914	Fukuo	M	19	Headache; signs of local and general compression	.....	3d ventricle; cystic	Squamous epithelium, cornified; hair; sebaceous glands	Connective tissue; fat; hyaline cartilage; bone with complete haversian	Columnar epithelium with gland formations of the gastrointestinal type	Complete formations of the wall of the upper gastrointestinal tract

									of the gastro-intestinal type	but complete picture is presented and illustrated by Berblinger	
8	1914	Fukuo	M	19	Headache; signs of local and general compression	.....	3d ventricle; cystic	Squamous epithelium, cornified; hair; sebaceous glands	Connective tissue; fat; hyaline cartilage; bone with complete haversian systems and bone marrow; smooth and striped muscle	Columnar epithelium with gland formations of the gastro-intestinal type	Complete formations of the wall of the upper gastro-intestinal tract
9	1915	Odermatt	M	10	Overgrowth; macrogenitalia; hypertrichosis; maturity	.....	Cystic	Squamous epithelium, cornified; pineal and nerve tissue	Connective tissue; cartilage	Columnar epithelium of the gastro-intestinal type	
10	1918	Meyer	M	11	Overgrowth; hypertrichosis; undernourishment; headache of sudden onset; signs of general compression	9 wk.	Over quadrigeminal plate; cystic; 4 cm.	Squamous epithelium, cornified	Connective tissue, hyalinized; cartilage; vascular spaces; smooth muscle	Columnar epithelium with cuticle cilia, goblet cell and papillary formations	
11	1919	Boehm	M	9¼	Head oversize at birth; overgrowth; hypertrichosis; macrogenitalia; maturity of voice and mental status; general apathy; headache; late signs of local and general compression; operation—puncture of the corpus callosum	5 yr.	3d ventricle; cystic; filled and distended 3d ventricle	Squamous epithelium, cornified and noncornified; enameloblastic organ; pineal, glial and ganglionic tissue; ependymal rosets; epithelioid cells of indifferent character	Connective tissue; hyaline cartilage; lymph vessels and follicles; smooth muscle	Columnar epithelium with gland formations of the gastro-intestinal and respiratory types	Congenital familial defects; tumor diagnosed as pineal teratoma on the basis of macrogenitosomia praecox. Tissue of note: (1) well formed structures of gastro-intestinal and bronchial walls; (2) dental buds but no enamel or dentine; (3) epithelioid cells of the interstitial type, as seen in the testis
12	1920	Frank	M	20	Headache; polydipsia; signs of local and general compression	4 wk.	Over quadrigeminal plate; cystic; 3.4×2.4×2.2 cm.	Squamous epithelium, cornified; pineal, glial and ganglionic tissue	Connective tissue, embryonal; cartilage; lymph tissues; smooth muscle	Columnar epithelium with glands of the gastro-intestinal and respiratory types bearing villi, crypts and acinic structures	Complete formations of gastro-intestinal bronchial and acinar units
13	1922	Klapproth	M	15½	Infantile habitus—adiposity; no pubic or axillary hair and small testes; headaches; lethargy; signs of local and general compression	6 wk.	3d ventricle; cystic; 4.4×2.8×3.6 cm.	Squamous epithelium, cornified; hair anlage; sebaceous glands; pineal tissue; adenomatous, ganglionic tissue and embryonal neuro-epithelial medullary tube formations	Connective tissue; fat; hyaline cartilage; membranous and lamellar bone; smooth muscle	Columnar epithelium with goblet cells	Infantile habitus; pineal adenoma with much mitosis; medullary neuro-epithelium

* The report of the case of Takeya (1913), that of a boy aged 15, repeatedly cited as a case of teratoma of the pineal body, is not available other than as quoted clinical data. Clinically the patient was said to have shown well established macrogenitosomia praecox. Histopathologic data were not given.

The growth in the case of A. J. McLean (1934), that of a boy aged 6, was a teratoma arising in the tela choroidea of the third ventricle, apparently taking origin in the parapineal structures. Anatomically the pineal body was not involved other than by compression. The possibility of an ontogenetic relationship to the pineal body causes the addition of this case to the series at this point. The report is noteworthy because of the successful operative removal of the tumor. (The patient died three hours after the delivery of the tumor.)

Case No.	Date	Author	Sex	Age, Yr.	Clinical Data	Duration of Illness	Location, Type and Size	Pathologic Picture			Comment
								Ectoderm	Mesoderm	Endoderm	
14	1934	Bochner and Scarff	M	9¼	Severe periodic frontal headaches; lethargy and vomiting with headaches; late signs of general compression Toothlike structures in roentgenograms	2 yr.	3d ventricle; cystic; 5.5×3.5×5.5 cm.	Teeth—adamantinomatous embryonal anlage and adult teeth, including dentine, dental pulp and enamel; hyperplastic pineal tissue; nerve tissue and glial structures	Connective tissue, embryonal and adult; hyaline cartilage; fat; membranous and lamellar bone with the haversian canals	Columnar epithelium with cuticle, cilia and goblet cell formations; simple and compound racemose glands and thyroid tissue	Tumor diagnosed as embryonal tumor (clinically) on basis of toothlike structures in roentgenogram; no metabolic disturbances. Tissues of note: (1) teeth, all forms from primitive to adult; (2) hyperplasia of pineal elements; (3) complete formations of mucosa of upper respiratory tract; (4) thyroid gland
					TERATOID TUMORS						
15	1911	Bailey and Jelliffe	M	12	Overgrowth; obesity; pallor; infantile status of voice and genitals; signs of local and general compression; patient mentally sluggish; calcified bodies in roentgenogram	10 yr.	Over quadrigeminal plate and in 3d ventricle; 1½ inch	Sebaceous material; hair	Cartilage	.....	"Dermoid" tumor
16	1921	Giebel	M	15	None given		Over quadrigeminal plate and in 3d ventricle; size of a walnut	Squamous epithelium, cornified; hair; hair follicles; sebaceous and sweat glands	Connective tissue	.....	.....
17	1925	Horrax and Bailey	M	3	Overgrowth; macrogenitalia; hypertrichosis; drowsiness; headache; signs of local and general compression	3 yr.	Over quadrigeminal plate and in 3d ventricle; cystic; 7×4 cm.	Squamous epithelium, cornified; hair; hair follicles; sebaceous glands; pineal anlage	Cartilage; bone; fat	.....	.....
18	1930	Altmann	M	11	Overgrowth; macrogenitalia; hypertrichosis; headache; drowsiness; signs of local and general compression	Few mo.	3d ventricle; cystic; 4.5×4×5.5 cm.	Squamous epithelium, cornified; hair; sebaceous glands	Connective tissue; cartilage; fat; lamellated bone	.....	Adult type of testes; early spermatogenesis
					NONDIFFERENTIATED TUMOR						
19	1906	Askanazy	M	19	Severe headache; signs of general compression	2 wk.	Over quadrigeminal plate; solid; size of a walnut	Pineal tissue; syncytial masses and single large cells with frequent mitoses	Vascular tissue, abundant	.....	Chorionepithelioma

TABLE 2.—*Data on Cases of Mixed and Doubtful Tumors of the Pineal Body Reported in the Literature* *

					compression		size of a walnut	and single large cells with frequent mitoses	

TABLE 2.—*Data on Cases of Mixed and Doubtful Tumors of the Pineal Body Reported in the Literature* *

No.	Date	Author	Sex	Age	Clinical Data	Duration	Location, Character and Size	Histopathologic Picture	Comment
1	1879	Falkson	M	16	Impaired memory and vision; signs of local and general compression	Since childhood	3d ventricle; cystic; 5.8×4.7×3 cm.	Sarcoma with cartilage; columnar epithelium-lined spaces, probably ependyma	Chondrocystosarcoma; mixed tumor of simple origin
2	1885	Ziegler	..	..	None given	.....	3d ventricle; cystic	Sarcoma with epidermoid carcinoma forming hyaline masses and columnar epithelium-lined spaces, probably ependyma	Mixed tumor of doubtful origin due to inadequate data
3	1885	Turner	..	..	None given	.....	3d ventricle; cystic	Sarcoma with columnar epithelium forming islands of carcinoma structure and ganglionic nerve cells	Mixed tumor of doubtful origin due to inadequate data
4	1887	Coats	M	13	Lethargy; signs of local and general compression	5 mo.	3d ventricle; 1⅞×1⅝×1¼ inches	Sarcoma with cartilage formation, columnar epithelium-lined spaces with goblet cells and "doubtful smooth muscle"	"Adenoid chondrosarcoma"—(the author's diagnosis). [He questioned the smooth muscle, and the presentation of columnar epithelium is not convincing]
5	1899	Ogle	M	6	Macrogenitalia; hypertrichosis; lethargy; signs of local and general compression	2 mo.	3d ventricle; cystic; 1 inch	Hemangioma with columnar epithelium-lined spaces, probably ependyma; cartilage and pineal tissue	Mixed tumor of simple origin
6	1899	Oestreich and Slawyk	M	4	Macrogenitalia; hypertrichosis; maturity of voice; colostrum expressible from the mammary glands; signs of local and general compression (Note—forceps delivery and convulsions at 1 yr.)	1 yr.	3d ventricle; cystic; size of small apple	Sarcoma with calcarious deposits and flattened epithelium, probably ependyma	"Psamocystosarcoma;" mixed tumor of simple origin
7	1913	Goldzieher	M	16	Hypertrichosis; severe headache; signs of local and general compression	3 mo.	Over quadrigeminal plate	Angioplastic sarcoma with syncytial masses	Simple tumor of highly anaplastic type
8	1914	Schmincke	M	19	Signs of general compression	.....	3d ventricle; size of large walnut	No specific data other than diagnosis of "tridermal teratoma"	Inadequate data; reported with case 9 as similar to it
9	1914	Schmincke	M	22	Signs of general compression; history of head injury 6 months previously	.....	Cystic; size of large walnut	Hemangioma with rudimentary ganglion cells, pineal tissue and columnar epithelium, probably ependyma	Mixed tumor, probably of simple origin; considered by author as a "tridermal teratoma"
10	1921	Luce	F	5½	Obesity; headaches; hydrocephalus; signs of local and general compression; calcified bodies in pineal region in roentgenogram; diagnosis of pineal tumor on the basis of roentgen findings	2 yr.	Over quadrigeminal plate	No specific data given other than that "cartilage" and "bony areas" were present	Considered as a "tridermal teratoma" by Professor Fahr, who reviewed the case

* Selected cases irregularly listed as embryonal tumors in past publications but here reclassified on the grounds of simple mixed or doubtful origins.

their cells possessed only that potentiality for further differentiation which was left in the already partially evolved epithelium from which they had taken origin.

Embryonal tumors which arise from the pineal gland present a decided contrast to the foregoing types of tumors, for there is much evidence to suggest that these tumors take their impetus to grow from a fundamental multipotentiality inherent in the primitive pineal cells.

The very complexity of an embryonal tumor of the pineal body, such as the one we shall describe, calls for the departure of the germinal cell groups very early in the life of the embryo, that is, close to the blastomere stage, whereas the pineal body does not appear as an entity until a much later date, that is, after the closure of both the dorsal and the ventral invagination. It is obviously difficult, if not impossible, therefore, to account for the location of cells in the pineal body which might have sufficient multipotentiality to produce such a complex tumor by any process of tissue inclusion or transplantation from the already partially formed integument.

Multipotentiality in an adult tissue is generally attributed only to cells found in the testis and the ovary. Numerous points of similarity, however, do exist between the pineal body and the testis, in both cell structure and neoplastic formation. The marked resemblance of the cell type of the pineal adenoma (pinealoma) to that of the spheroidal cell tumor of the testis (seminoma) has been stressed by Harris and Cairns. Van den Bergh and also Boehm have reported finding in pineal teratomas "epithelioid cells of an indifferent character" having the essential characteristics of the interstitial cells of the testis. Actual chorionepithelial elements in tumors of the pineal body have also been described by Askanazy and by van den Bergh. The pineal body ranks second to the testis as a source of multipotential neoplastic material, and together they form the principal locations of teratomas in the male.

Finally, the multipotentiality of the primitive pineal cells is further attested by the comparative embryology and anatomy of that body. It has formed an eye in the cyclostomes, racemose glands in some birds and the structure of an endocrine gland in the mammal.[2]

CLINICAL MANIFESTATIONS OF PINEAL TUMORS

The clinical manifestations of tumors of the pineal body fall into two groups, the mechanical and the constitutional (or endocrine).

Mechanical obstruction of the ventricular system gives rise to the classic symptoms and signs of increased intracranial pressure. A peculiarity of diagnostic value, at times encountered in tumors of the

2. This thesis has been presented repeatedly by Tilney; see his text and the discussion following the paper on "Pinealomas" by Globus and Silbert.

third ventricle, is an intermittent abrupt increase of signs of pressure caused by the valvelike action of the free lying tumor in the narrow third ventricle. This mechanism (described by Stookey and others) is responsible for the recurrent midfrontal headaches and drowsiness which are so often the first and, as we have seen in our own case, may be the only complaint of the patient. Pressure on the quadrigeminal plate is the usual source of whatever localizing signs may be presented by these tumors. There is then produced the well known picture of drooping eyelids, difficulty of upward rotation of the eyeball and occasionally an Argyll Robinson pupil. Frequently focal signs are entirely lacking, and this fact in itself, in the presence of greatly increased intracranial pressure, has decided diagnostic value and should arouse suspicion of a tumor of the third ventricle or of the pineal body.

The constitutional manifestations of tumors of the pineal body are inconstant. Nevertheless, when they are present they form a picture so striking and of such great diagnostic value as to deserve special consideration as a symptom complex. There is a remarkable precocity in the somatic, genital and psychic development, with actual maturity of outlook and function. Pellizzi described the phenomenon as "macrogenitosomia praecox." This syndrome has been described (at least in part) in nine of the nineteen reports of true embryonal tumor in the literature.[3] In the far more numerous simple and mixed tumors of the pineal body the phenomenon has been noted only ten times.[4]

MACROGENITOSOMIA PRAECOX

The association of pathologic conditions of the pineal body with sexual and somatic overgrowth has led to much discussion and to two principal theses.

Marburg contended that the pineal body is a functional part of the endocrine chain, acting specifically to inhibit maturation. He pointed out that the first manifestations of puberty appear with the involution of the pineal body. Further, it is noteworthy that macrogenitosomia praecox has been fully established only in preadolescent males, that is, prior to the natural involution of the gland and at a time when the function of the pineal body has been prematurely inhibited. Experi-

3. This includes the incomplete case report of Takeya.

4. The following authors have reported the ten recorded cases of pineal tumors, other than embryonal tumors, in which macrogenitosomia praecox has been manifest. These cases are given no further consideration in this paper, and the reader desiring further information is referred to the original works—see bibliography: Ogle, hemangioma; Oestreich and Slawyk, psammocystosarcoma; Holzhäuer, psammocystosarcoma; Raymond and Claude, neuroglioma; Goldzieher, angioplastic sarcoma; Horrax, pineal adenoma; Skoog, pineal adenoma; Lereboullet et al, neuro-epithelioglioma; Tilney and Riley, pineal "tumor," and Steiner and Johan, pineal adenoma.

mental evidence as to the endocrine function of the pineal body has been irregular but of sufficient interest to be noted here. Foa removed the pineal bodies in chicks from 11 to 93 days of age. He found an increased rate of development from two to five months after the operation, and at from eight to fifteen months (at autopsy) there was demonstrated a decided overgrowth of both testes and combs. Horrax pinealectomized guinea-pigs and also found an overgrowth of the testes at autopsy. On the other hand, Dandy, working on dogs, and Anderson and Wolf, using rats in a carefully conducted series, found that the operation had no influence on sexual development (Dandy) or on the rate of growth, age of puberty or weight of other endocrine organs (Anderson and Wolf). Rowntree and his co-workers injected pineal extract (Hanson) into the peritoneal cavities of rats daily for five generations. They noted a decided retardation of the rate of growth and an acceleration of the rate of development and maturation.

Askanazy considered the phenomenon of macrogenitosomia praecox as a "pseudo-pregnancy state" induced by the presence within the body of an embryonal tumor. He cited the case of Sachi, in a boy of 9 years, in whom since the age of 5 skeletal overgrowth and changes in the voice had developed. The testicular tumor, which proved to be a teratoma, was removed, and shortly thereafter the boy returned to a normal preadolescent state. Experimental support of this thesis is offered by Starling, who injected the products of macerated rabbit embryo into immature female rabbits and produced precocious sexual overgrowth and maturity. The more recent development of the Aschheim-Zondek phenomenon as a test for pregnancy, or rather for the overflow of hormones associated with pregnancy, has led to the startling finding that the urine of a person bearing an embryonal tumor will induce (apparently in the same manner) precocious maturity in immature female rabbits.[5] These findings are entirely in keeping with the observed greater incidence of precocity in cases of true embryonal tumor of the pineal body, but obviously do not entirely answer the problem.

Our patient, although bearing a highly complex teratoma of the pineal body, failed to show any of the characteristic features of macrogenitosomia praecox. The difficulty in attempting to establish an exact relationship between a pathologic process of the pineal body and sexual

5. Zondek found that the urine of a person with a malignant growth, and more particularly a malignant growth of the genitals, frequently gave a positive reaction for a follicle-stimulating hormone—in 81.8 per cent of cases of malignant growths of the genitals and in 20.4 per cent of cases of extragenital malignant growths. Ferguson studied 117 cases of teratoma of the testes and established the importance of the quantitative test for a follicle-stimulating hormone in the differential diagnosis of tumors of the testes.

activity is further well illustrated by Klapproth's case, in which a teratoma of the pineal body was combined with extensive hyperplasia of the pineal body. In this case the patient, a 15½ year old boy, was sexually infantile. It may be seen that while the existence of a relationship between activity and pathologic changes of the pineal body and the sexual function is probable, the nature of this relationship is far from established.

DIAGNOSIS

The ultimate clinical diagnosis of embryonal tumor of the pineal body usually must depend on ventriculographic and roentgenographic studies. Shadows of calcified bodies, when present, have great diagnostic value. The phenomenal appearance of formed teeth, as seen in the roentgenograms in our case, is, of course, pathognomonic. The manifestation of macrogenitosomia praecox or a positive reaction to the Aschheim-Zondek test in a patient suspected of having a tumor of the pineal body has the weight of deciding evidence in favor of a diagnosis of pineal teratoma.

TREATMENT

Early surgical removal of the tumor is the only complete form of treatment. The mid-dorsal approach, splitting the corpus callosum, as described by Dandy in 1921, is the most usual. Van Wagenen in 1931 described a lateral approach across one of the dilated lateral ventricles. Detailed description of the procedure and analysis of results are discussed by both Dandy and Van Wagenen.

REPORT OF A NEW CASE OF TERATOMA OF THE PINEAL BODY

History.—J. S., a boy aged 9¼ years, was admitted to the New York Post-Graduate Hospital on May 7, 1933, complaining of headache and drowsiness. He was the fourth child of an apparently normal and healthy family. Gestation and birth were uneventful. Physical and mental development during infancy and childhood were well balanced, and the child's conduct and class standing at school were excellent.

When the patient was 7 years of age (in the fall of 1931), remarkably well localized midfrontal headaches made their appearance. Later these were associated with an intense desire for sleep, lasting for about an hour, after which he would arise entirely relieved and to all intents and purposes again be a normally active boy. He came to the outpatient department of the hospital on Nov. 27, 1931, complaining of headaches. Sinusitis was found and treated, with marked symptomatic improvement. It is of note that the visual acuity and optic fundi were reported as normal at this time.

Attacks of headache and lethargy reappeared during the spring of 1932, more severe and often accompanied by nausea and vomiting. It was later noted that rough or long rides in a motor car would induce an attack. The boy returned to the clinic in September 1932 because of the increasing frequency of these attacks. Roentgen studies of the head at this time showed a remarkable series of calcareous bodies in the area of the interbrain. Neurosurgical consultation was advised on

the grounds of a probable tumor of the third ventricle, but this action was postponed by the family because of temporary symptomatic improvement.

Occasional attacks during the period between September and the following May, although severe, did not greatly interfere with the patient's daily routine. He was able to continue at active work and play until May 7, 1933. On that morning he complained of headache and sleepiness more marked than usual. Two hours later his mother found him still apparently asleep but very pale. She had great difficulty in arousing him. That evening, because of the persistence of this semistuporous state, he was taken to the hospital.

Fig. 1.—The patient (with bat) at play with his brothers, two weeks prior to his death at the age of 9¼ years.

Physical Examination.—The boy was found to be well developed, drowsy and apathetic. The fundi showed early bilateral papilledema. The deep reflexes were diminished, and Babinski and Chaddock signs were present bilaterally. Examination, as far as it could be carried out at that time, otherwise gave negative results.

The following morning he seemed somewhat better. Roentgenograms of the skull showed evidence of increased intracranial pressure as well as the calcified bodies in the area of the interbrain. It was noted that these calcified bodies bore a remarkable resemblance to the nonerupted teeth to be seen in the mandible. A clinical diagnosis of embryonal tumor of the area of the interbrain, probably

of the third ventricle, was made, based in part on the history but to a large extent on the most unusual roentgenographic findings.

Careful questioning of the family failed to reveal any evidence of metabolic or developmental disturbance at any period in the boy's life. There was neither polydipsia nor polyuria (no enuresis) and no olfactory, visual or auditory disturbances. His height at the age of 9 years (three months before admission) was 4 feet and 10 inches (147.3 cm.). His last observed weight, at the age of 7 years, was said to have been 61½ pounds (27.9 Kg.). His general physical proportions had always been those of a normally active boy of his age. Neither parent had

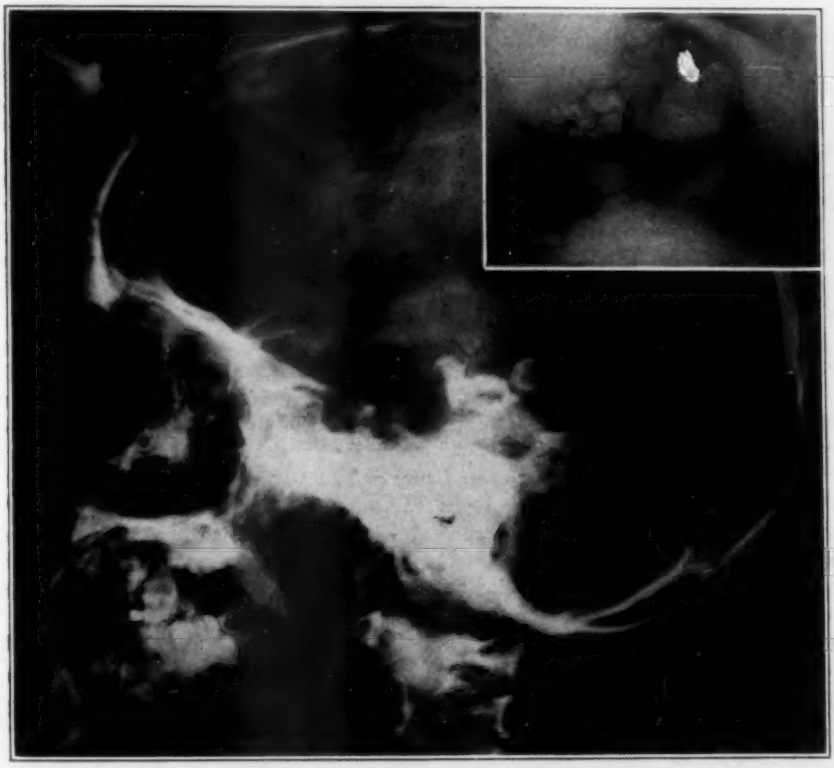

Fig. 2.—Roentgenogram of the head showing shadows of the teeth in the area of the interbrain. The insert is a roentgenogram of the brain made at autopsy. Note the similarity between the shadows in the area of the midbrain and the non-erupted teeth of the jaw.

observed anything unusual about the development of his secondary sexual characteristics.

Clinical Course.—The clinical course in the hospital was marked by periods of mild headache and drowsiness. Between these attacks the patient felt fairly well, so that the critical nature of his condition was not properly appraised. On May 12, however, at 5:30 p. m. there occurred a series of short convulsive attacks characterized by twitchings of the extremities and grating of the teeth and followed by

dilatation of the pupils and marked irregularity of the pulse. There were cyanosis and an irregular Cheyne-Stokes type of respiration. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously, after which the pulse and respirations became essentially normal, and the child's appearance was much improved. Immediate trephine and ventricular tap were decided on in order to combat the acute phase of intracranial pressure. The child, seemingly in fairly good condition, was being gently lifted from the bed to the stretcher when respiration ceased. All attempts at resuscitation failed.

Necropsy.—Gross Examination: The body was that of a well developed rather well nourished boy. The skin was smooth and soft, bearing no pubic or axillary hairs. The head was covered with a normal growth of light brown hair. The external genitalia appeared normal in all respects. The testicles were descended.

The examination was limited by the family to the head. The scalp stripped readily. The calvarium raised with little difficulty, though the dura was moderately adherent thereto. The brain was removed, revealing a not remarkable cranial base. The venous sinuses contained soft postmortem thrombi. The ethmoid and sphenoid sinuses were free from purulent material. The middle ears were not remarkable. The brain was symmetrical and well formed and weighed 1,535 Gm. The pia-arachnoid was markedly engorged. The basilar vessels were normal in structure and arrangement. The gyri were decidedly flattened and the sulci narrowed. Bulging of the floor of the third ventricle was apparent, raising and flattening the optic tracts. The hypophysis was not involved.

Coronal and midsagittal sections, made through the area of the interbrain, revealed a large cystic tumor filling and greatly distending the third ventricle. The foramina of Monro, though enlarged, were occluded by the position of the tumor mass, with resultant hydrocephalic distention of the lateral ventricles. The tumor mass measured 5.5 by 5.5 by 3.5 cm. in its greatest diameters. It extended forward to displace the anterior commissure and backward to overlie and compress the quadrigeminal plate. The corpus callosum and splenium were raised and attenuated. The thalami were displaced and compressed to caplike structures. The body of the tumor lay free in the cavity of the third ventricle but for its anchorage at the region of the telae and the pineal body. The recess of the pineal body was identified, but no vestige of the pineal body was recognized. The aqueduct of Sylvius was patent, though the quadrigeminal plate was much flattened.

The tumor was made up of two principal portions, the posterior and larger portion being a firm, grossly nodular cystic mass, and the anterior portion, a large single thin walled cyst. The cyst was smoothly lined and filled by a milky limpid fluid. The structure of the mass was of a firm fibrous tissue, riddled by intercommunicating cysts and channels. These spaces contained a milky fluid similar to that of the large anterior cyst and were similarly smoothly lined. Just to the left of the midline there was a series of bony hard bodies loosely fixed in shell-like capsules. They had the general appearance of well formed teeth. The largest of these measured 7.5 mm. in diameter and presented two well formed cusps. The lower portion of the tumor was largely made up of an irregular soft structure. An extension of this softer material formed a horizontal mound over the entire rear portion of the tumor, lying on and compressing the quadrigeminal plate. On this mound and extending over its entire length, there was a collapsed saclike structure, which when distended measured 1.5 cm. in diameter. The sac was blind on the left, and on the right it was continuous with the chain of cystic spaces of the denser portions of the tumor.

Microscopic Examination: Frozen and paraffin sections were prepared and stained by hematoxylin and eosin, Van Gieson stain for connective tissue, sudan III

Fig. 3.—Gross sections of the brain passing through the central portion of the tumor mass. Note the marked compression of the surrounding structures, the irregular cystic character of the mass and the encapsulated tooth structures.

Fig. 4.—Low power photomicrograph showing the general structure of the tumor mass. Note the wide variety of tissue structures—cysts, glands, fat, bone and pineal and fibrous tissues. Hematoxylin and eosin stain.

for fat, Hortega's silver carbonate for neuroglia and Bielschowsky and Plien's stain for nerve cells.

Connective tissue stroma of varying density formed the larger portion of the tumor mass. In some areas it was fibroblastic, in others the tissue was more mature, even forming dense collagenous and hyalinized bands. Areolar tissue was widely spread throughout the mass and similarly presented both young and mature cell formations.

The tooth structures noted in the gross specimen showed all stages of dental evolution, ranging from the primitive ameloblastic ridge to completely formed multicuspid teeth. Irregular dental bud elements formed arrangements typical of the adamantinomas of the craniopharyngioma or suprasellar cyst group. There was the typical central mass of loosely scattered small stellate cells, bordered by a ribbon of flattened intermediate cells and the tall clear palisade of ameloblasts. In areas the structure took on the more regular arrangement of the dental bud, forming a hood to the richly vascular dental pulp. The pulp was formed of rather large compactly arranged stellate cells having the general appearance of fibroblasts. The invaginated portion of the layer of ameloblasts was of larger cells and formed the inner enamel epithelium. The outer ribbon of ameloblasts was atrophied and formed the flattened cells of the outer enamel epithelium. At one point the outer enamel epithelium became thickened, forming a mound of large cuboidal primitive ameloblasts—the secondary dental germ structure. The layer of odontoblasts had similarly been differentiated from the dental pulp along its line of contact with the inner enamel epithelium. The odontoblasts formed the typical palisade of tall columnar cells, having well defined cuticular margins and the usual basilar irregularity. The more matured dental structures had a layer of dentine deposited over the row of odontoblasts as a homogeneous pink-staining and finely lamellated structure. Well formed homogeneous enamel substance surmounted the dentine. The ameloblastic organ of the mature tooth appeared as atrophic strands, whereas the dental pulp, on the other hand, had become more prominent and more vascular, forming the permanent dental pulp body. No root structures had developed, although a number of bony spicules were present at the bases of the fibrous dental capsules. Six completely formed teeth were recognized. There were many others, more irregular, both complete and fragmentary, to be seen in a series of sections. Stained with hematoxylin and eosin, the dentine appeared red and the enamel blue; with Van Gieson stain, the dentine was a deep red and the enamel a yellowish brown.

Osteoid tissue and a number of foci of primitive membranous bone formations were frequent. The bony spicules were richly bordered by deeply staining polygonal osteoblasts as well as occasional large mononucleated and multinucleated osteoclasts. More compact masses of mature lamellar bone were present, in large part showing complete haversian systems and readily identified periosteum. Masses of noncalcified richly cellular hyaline cartilage were bordered by well defined perichondrium.

Epithelium, characteristic of the gastro-intestinal and respiratory tracts, formed the lining of the many cysts and spaces. This was for the most part made up of a tall palisade of ciliated cells having well defined cuticular borders. Goblet cells were numerous and were for the most part distended by a clear foamy material, apparently mucinous. In some areas the cells were flattened and irregular; nevertheless the fundamental cell type was similar throughout. Underlying the epithelial layer there was a condensation of fibrous stroma, which in areas had the appearance of hyalinized smooth muscle. Van Gieson's stain, however, indicated the mesenchymal character of the structures.

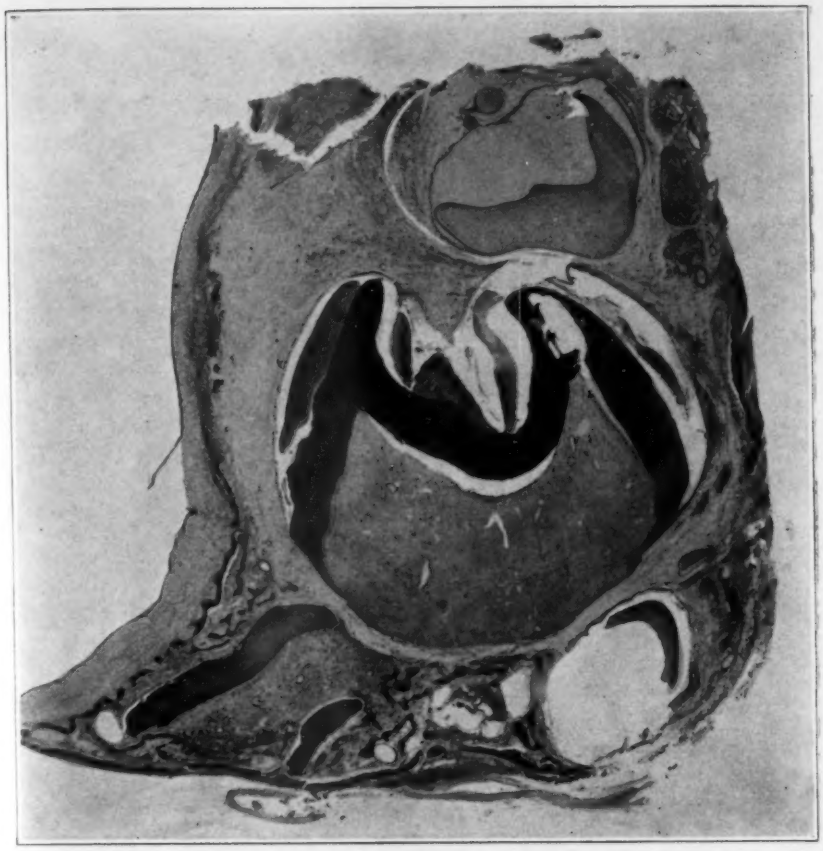

Fig. 5.—Low power photomicrograph showing the tooth-bearing area of the tumor. Note the serial generations of primitive and adult structures—dentine, dental pulp and enamel and the dental bud of the enameloblast organ. Hematoxylin and eosin stain.

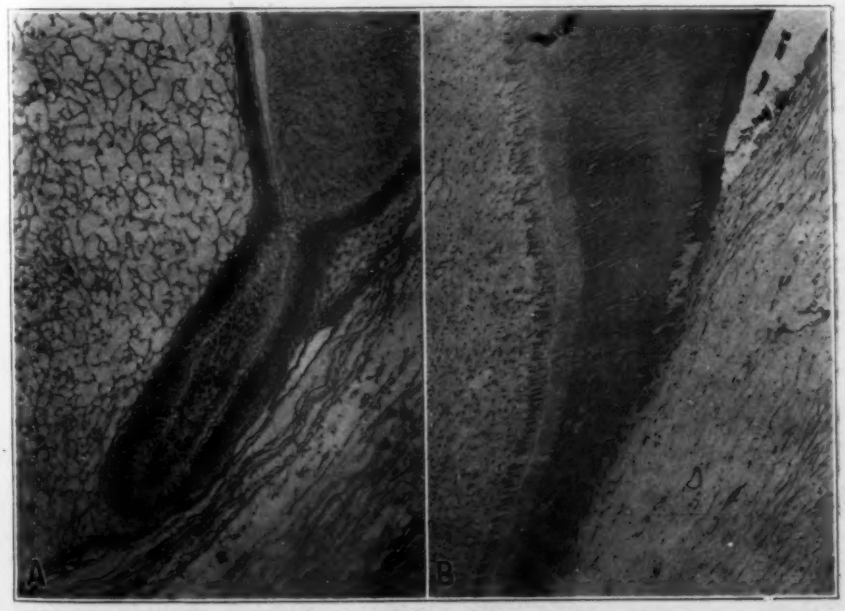

Fig. 6.—High power photomicrographs of the tooth-bearing area. *A* shows the ameloblastic layer of the enamel organ, which had undergone adamantinomatous formation. *B* shows the dentine body with pulp, a layer of odontoblasts and dentine. Hematoxylin and eosin stain.

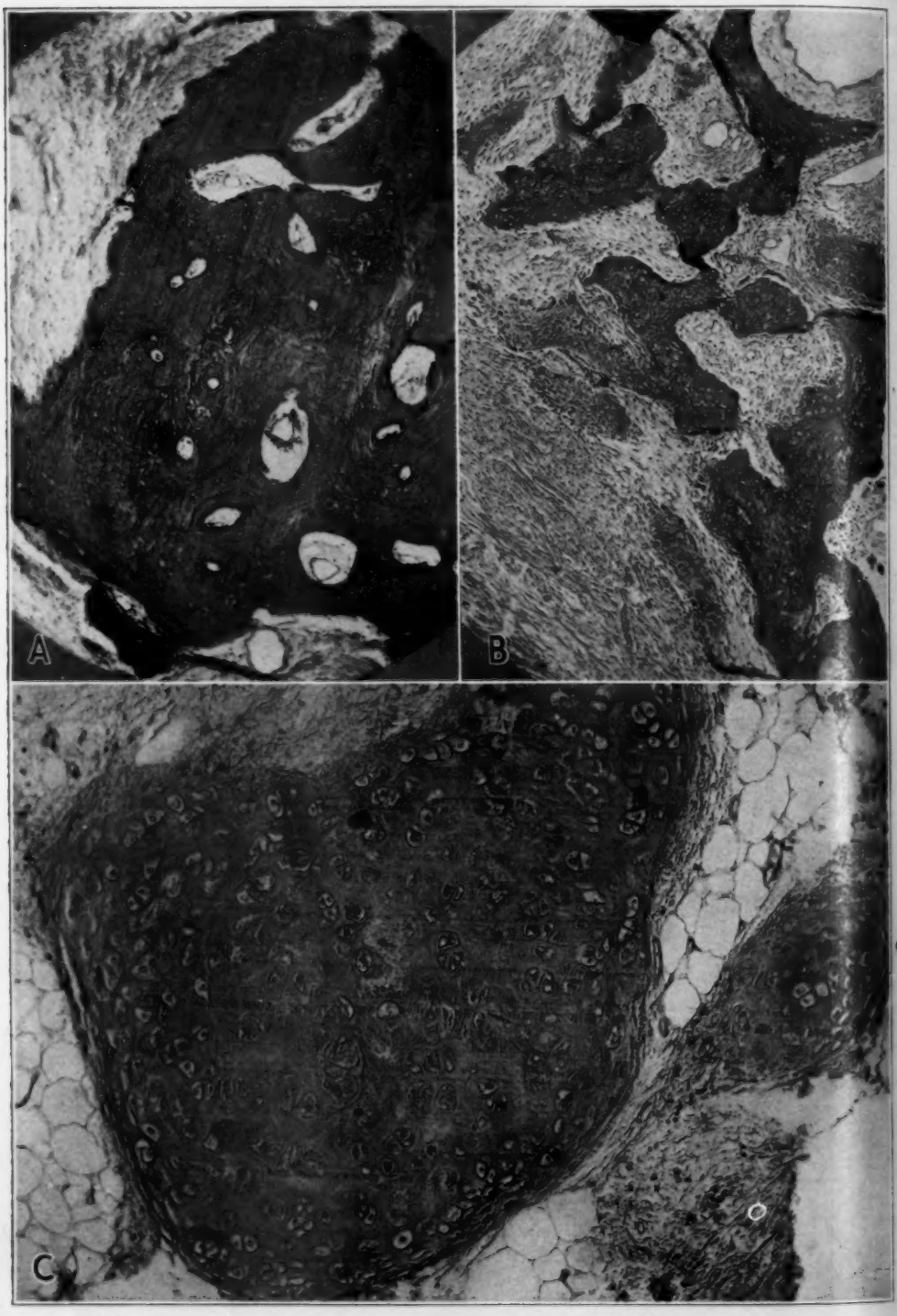

Fig. 7.—High power photomicrographs of sections showing bone and cartilage formation. *A* shows lamellar bone; note the haversian system and the periosteum. *B* shows membranous bone; note the osteoblastic activity. *C* shows hyaline cartilage; note the perichondrium and fibro-areolar tissue.

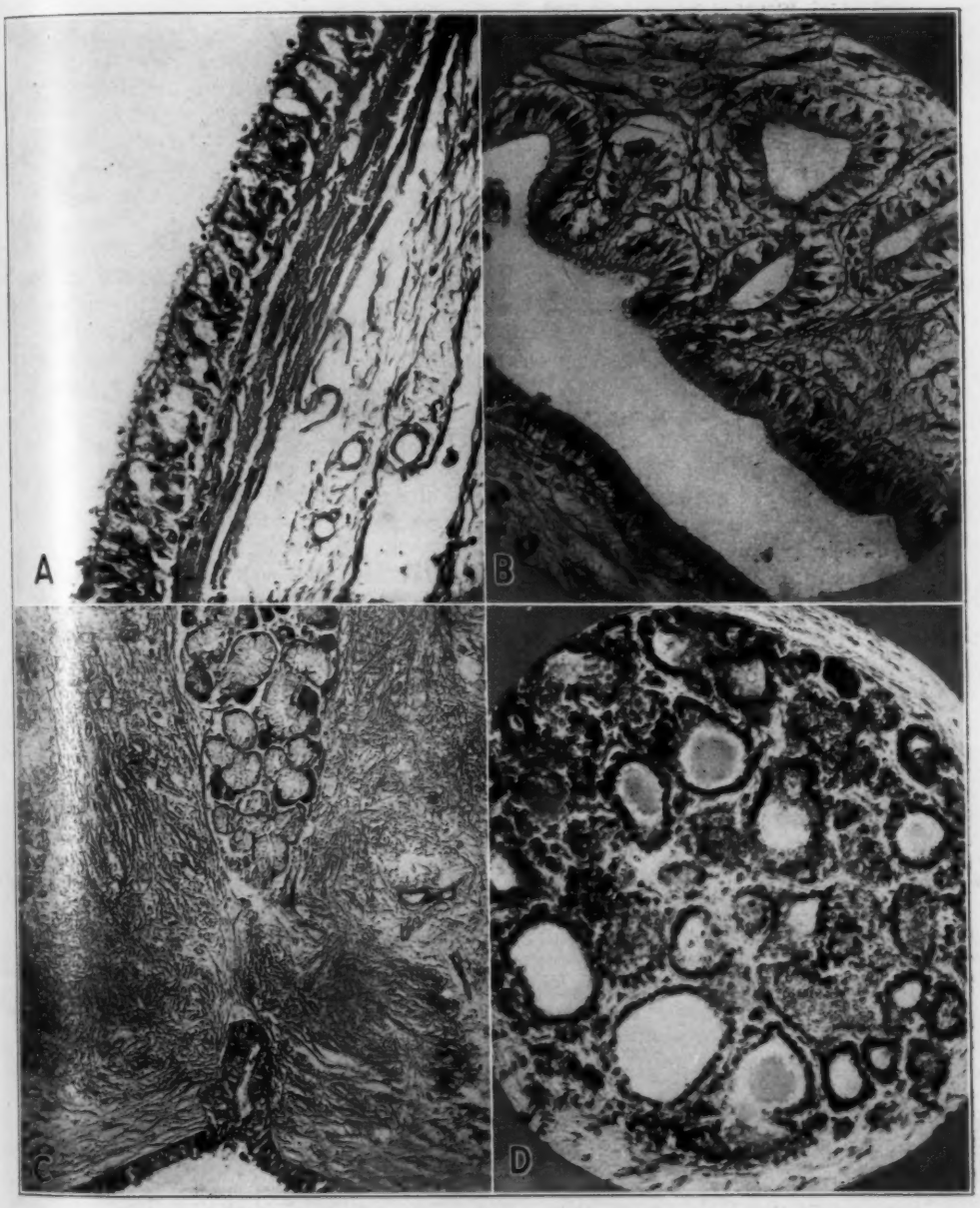

Fig. 8.—High power photomicrographs of sections showing epithelium and gland formation. In *A*, the section showing columnar epithelium, note the cuticle, cilia and goblet cells. Tubular gland formation is seen in *B*. In *C*, the section presenting compound racemose glands, note the mucinous acini and serous demilune groups, as of the mixed salivary glands. Thyroid gland formations are seen in *D*. Hematoxylin and eosin stain.

There was much glandular tissue, in places showing direct origin from infoldings of the epithelium lining the cystic spaces. These varied from the simple tubular to the compound racemose architecture of the mixed seromucinous type. The latter structures closely resembled submaxillary salivary glands, being made up of mucinous acini and serous "parietal" or "demilune" collections of cells. The tissue, on the whole, closely simulated the active mucosa of the upper respiratory tract, particularly that of the nasopharynx.

Thyroid tissue formed two isolated islands of acinous structure. The epithelium lining the well rounded acini was of the typical cuboidal type, possessing large well rounded nuclei. Many of the acini were filled with homogeneous pink-staining colloid, characteristically retracted.

Nerve tissue elements were widely scattered throughout the tumor. The more abundant collections formed the softer areas noted at the gross examination at the lower portion of the tumor. The glial cells were largely astrocytes, although glioblasts were not infrequent. A number of giant astrocytes were made out, some multinucleated. Nerve cell bodies were abundant, both as the rounded ganglionic form and as the large pyramidal form. The cytoplasm was ample and for the most part rather granular. The nuclei were well defined and rounded and contained sharply outlined and deeply stained nucleoli. Straight nerve fibers were seen to leave the cell bodies and in places to run for some distance in the plane of section. The numerous small islands and strings of neural elements, scattered through the fibrous stroma of the mass, were placed in sharp contrast by the Van Gieson stain.

Pineal structure, in its characteristic mosaic of large and small cells, was found as scattered groups throughout the hindportion of the tumor mass. Occasional small laminated calcareous nodules, psammoma bodies, were found in these areas. There was, however, no further evidence of involutionary change, as might be expected at the age of 9 years; rather the richly cellular character and the distinct mosaic formation were typical of the pineal gland as seen in infancy and in early childhood. Further forward in the tumor and closely associated with the widely scattered neural elements, there were numerous irregular groups of round cells. These cell groups, though not presenting the same mosaic formation, were strongly suggestive of the pineal element. They were largely made up of the smaller cell type, although there were some scattered larger cells, singly and in small groups, an arrangement found in the midfetal pineal body.

ANALYSIS OF THE CASE REPORT

The diagnosis of teratoma was established primarily by the embryonal nature of the neoplasm and secondarily by its tridermal character. The structure of the tumor was such that it must necessarily have arisen from a primitive cell group which had been isolated during early embryonal life and had later differentiated in the direction of its retained potentiality. The tridermal character of the neoplasm was richly manifest in both embryonal and adult tissue structures. Ectoderm contributed nerve cell and axonal structures, neuroglia and pineal and dental elements. Mesoderm formed the connective tissue stroma, cartilage, areolar tissue and osteoid, membranous and lamellar bone. Endoderm formed the ciliated columnar epithelium and glandular structures of the upper respiratory tract and the thyroid gland.

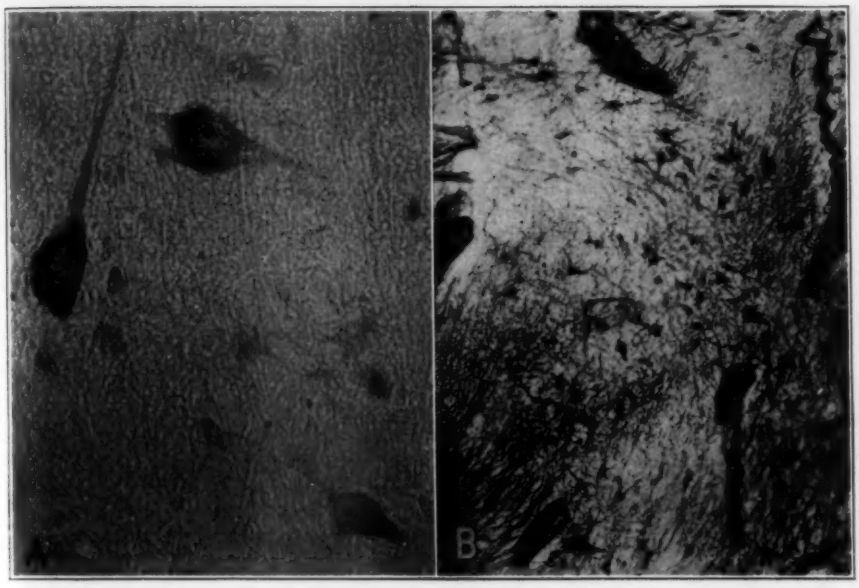

Fig. 9.—High power photomicrographs showing nerve and glial formations. Pyramidal and ganglionic nerve cells are seen in *A* and astrocytes, showing typical foot-plate formations, in *B*. Bielschowsky and Plein's stain for nerve cells and the Hortega stain, Globus modification, for neuroglia.

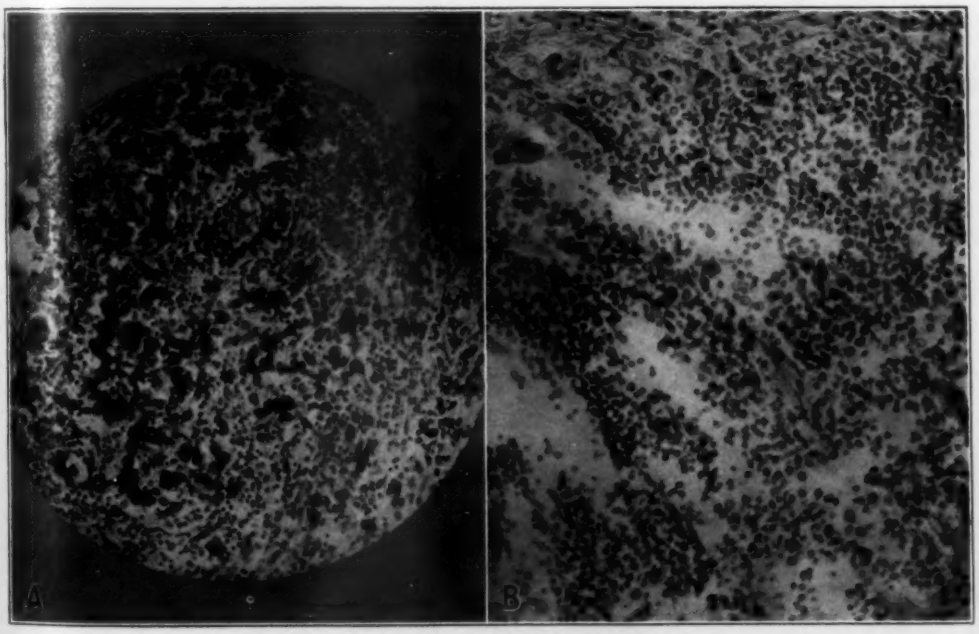

Fig. 10.—High power photomicrograph of the pineal structure. *A* is an area in the posterior portion of the tumor mass. Note the streams of large and small cells and the relative absence of involutionary changes. *B* is an area in the anterior portion of the tumor mass; note the predominance of small cells. Hematoxylin and eosin stain.

The pineal origin of the neoplasm was evidenced on gross examination by its anchorage at the site of the pineal body and complete replacement of that body and on microscopic examination by the finding of pineal tissue, of the type generally found in infancy, as an integral part of the tumor mass.

Teeth, in all stages of their development, formed the unique feature of this case and are here reported for the first time in a teratoma of the pineal body. The progressive serial relationship of the primitive dental buds to the mature well formed teeth gives the complete picture of dental evolution. In the available literature, considering all types of intracranial neoplasms, there is but one other case in which adult tooth structures are described, and that is a case of teratoma of the pituitary body reported by Hugo Beck.[6] Boehm reported a case of teratoma of the pineal body in which he found elements of the primitive enamel organ, but there were no evolved tooth structures. Ameloblastic cell groups without further dental formations are frequently present in craniopharyngiomas (suprasellar cyst, adamantinoma and ameloblastoma). This is not remarkable in view of the fact that these neoplasms take origin from the vestigial remains of the craniopharyngeal (craniobuccal) canal. The most recent comprehensive collection and analysis of craniopharyngiomas is that of Frazier and Alpers. They illustrated ameloblastic elements of the primitive enamel organ, but nowhere did they find evidence of true enamel formation. Peet described an irregular "pseudo-enamel" in an adamantinoma of the pituitary body. McLean mentioned "two areas bearing resemblance to an early enamel organ" in a parapineal teratoma.

Neural elements have repeatedly been found in teratomas of the pineal body, both as immature ganglionic structures and as well formed nerve cells and fibrils. Klapproth reported embryonal medullary epithelium in his case of a teratoma of the pineal body. Neuroglia is less common and is reported only by Boehm, Frank and ourselves.

The teratoma in its evolution may destroy the pineal tissue, may include it within its structure or may give rise to pineal tissue as new growth material. Klapproth reported adenomatous hyperplasia of the pineal body as an integral part of the teratoma. The immature pineal tissue so widely dispersed throughout our tumor, though not as abundant or as actively proliferating as in the case of Klapproth, is apparently of the same nature. The intimate association of the pineal and

6. R. A. C. Rigby has published roentgenograms of a skull showing a suprasellar cyst with shadows which he interpreted as teeth. However, his report is accompanied by neither anatomic nor pathologic data. He cited Bonorden as reporting a tumor of the olfactory area with fourteen teeth. This is evidently an error, as Bonorden's report describes a cyst containing squamous epithelium, hair and sebaceous glands but does not mention teeth.

the neural elements throughout the tumor is remarkable and of considerable interest in view of the existing controversy as to the association of these elements in the normal pineal gland and in neoplasms of the gland.[7]

Squamous cornifying epithelium and its associated skin appendages are the most commonly found ectodermal elements within embryonal tumors. Singularly enough, they were not present in our case.

The endodermal derivatives in our case formed structures characteristic of both the nasopharyngeal wall and the thyroid gland. These forms are unique in that they have not been reported in any other teratoma of the pineal body. Well formed structures of the esophageal and gastric walls are reported by Fukuo, Odermatt, Boehm and Frank. Frank reported actual villus formation, as of the small intestine. Bronchi and respiratory epithelial group formations are described by Boehm and by Frank.

In establishing the endodermal character of epithelium-lined spaces, it is essential to demonstrate an association of tissue patterns at least sufficient to be recognized as a part of an endodermal organ. The necessity of such a criterion was stressed by Marburg, because he was able to illustrate beyond question the transition of characteristic ependyma into columnar ciliated epithelium with actual goblet cell formations. It is evident, therefore, that simple epithelium-lined spaces, as found in compound or mixed tumors, may be of no significance other than as ependymal inclusions.

Osteoid and primitive membranous bone are uncommon findings in pineal teratoma. True lamellar bone is still more infrequent. The latter structure is reported by Fukuo, Klapproth and ourselves. Klapproth also reported the presence of myeloblastic tissue of the bone marrow. Cartilage was found in abundance in the case reported here and also in other such tumors reported in the literature.

Striped muscle has been reported in but two cases, those of Neumann and Frank. Smooth muscle is more frequent and in most instances is found in gastro-intestinal or respiratory (bronchial) complexes; neither type of muscle structure was found in our case. Areolar tissue, so frequent in our case, is rather uncommon in the reports of other cases of pineal teratoma.

SUMMARY

Definition and classification of embryonal tumors have been given, with special attention directed to those of the pineal body.

The literature has been reviewed, and all recorded cases of embryonal tumor of the pineal body have been analyzed and reclassified.

7. The reader is referred to the papers of Horrax and Bailey and of Globus and Silbert and to the discussion following these papers.

The thesis is advanced that the impulse for embryonal tumor formation within the pineal body originates in an inherent multipotentiality in the primitive cells of the pineal body similar to that found in cells of the testis and ovary.

The clinical features of embryonal tumors of the pineal body have been reviewed, with especial emphasis given the syndrome known as "macrogenitosomia praecox."

A new case of teratoma of the pineal body is here reported in which a unique feature is the presence of teeth in all stages of development up to the adult forms. Such formations have not been reported in teratomas of the pineal body prior to this time. Similarly unique formations are seen in the extensive development of structures identified with the nasopharynx and with the thyroid gland.

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METASTASIZING HEMANGIOMA SIMULATING AN ANEURYSM

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Hemangiomas are generally regarded as benign tumors of the blood vessels. Passing reference to a rare form exhibiting malignancy clinically and giving rise to distant metastases is made in most of the standard works on tumors. Isolated cases of this sort have appeared from time to time.[1] Wright[2] in 1928 reported an additional case and reviewed the literature. In the recorded cases the breast, liver, lungs and pleura, intestines, spleen, kidney, heart, adrenal glands and subcutaneous tissues have been involved. Because of the unusual clinical form as well as the rapid recurrence of the tumor and metastasis in spite of intensive irradiation, the following case seems worthy of being placed on record.

REPORT OF A CASE

An 82 year old white man was admitted to the Johns Hopkins Hospital on March 29, 1936. He had had a small lump in the hypothenar region of his right hand for approximately fifteen years. The lump had been entirely painless and had given him no concern until three months before admission, when it suddenly began to increase in size and became painful. There was a history of trauma. Examination showed an extremely well preserved man of advanced years. On the hypothenar eminence of the right hand there was a rounded swelling 4 cm. in diameter. This mass was tightly attached to the skin and was not movable over the palm, but a definite arterial pulsation was felt. No murmurs were heard. The ulna artery above the tumor was twice the size of the corresponding artery in the left wrist and gave a forceful pulsation. The right ulnar artery was twice the size of the right radial artery. The epitrochlear nodes were not palpable. A small soft gland was palpable in each axilla.

From the Department of Surgery of the Johns Hopkins University Medical School.

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2. Wright, A. W.: Primary Malignant Hemangioma of the Spleen with Multiple Liver Metastases, Am. J. Path. **4**:507 (Nov.) 1928.

The heart was markedly enlarged to the left, and a loud systolic murmur was heard over the aortic area. The blood pressure was 180 systolic and 100 diastolic; the peripheral vessels were tortuous and thickened. The results of the rest of the physical examination were in keeping with the age of the patient, but no striking abnormalities were noted. The hemoglobin content was 98 per cent; the white blood cell count was 8,900 and the Wassermann reaction was negative. A roentgenogram of the hand showed a large soft tissue mass, which was homogeneous and not calcified. An electrocardiogram showed evidence of moderate myocardial damage. Aspiration of the mass with a small needle easily yielded blood. A preoperative diagnosis of aneurysm of the ulnar artery was made.

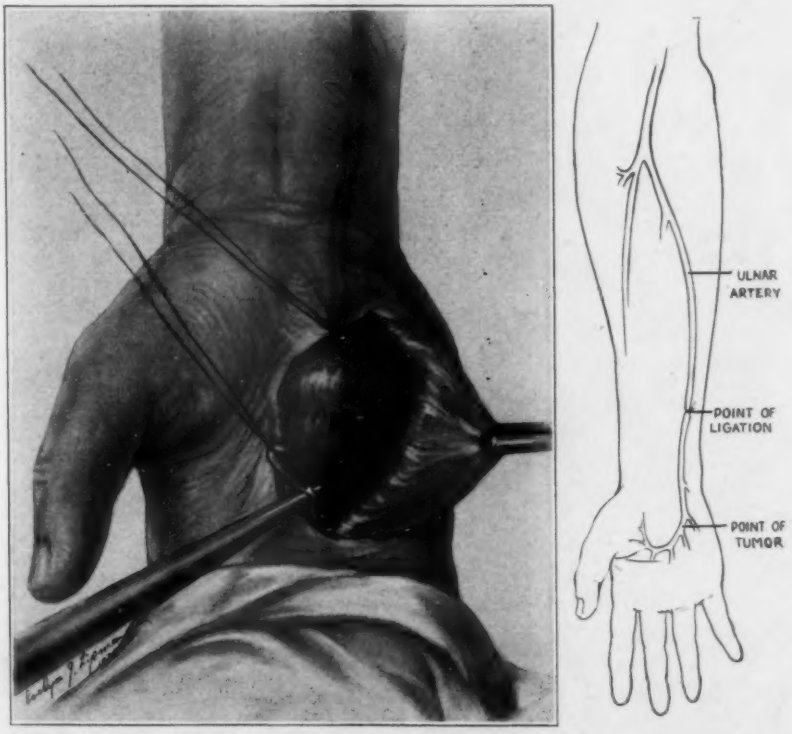

Fig. 1.—Sketches made at operation to indicate the position of the lesion.

On April 1 operation was performed, brachial plexus anesthesia being induced with 2 per cent procaine hydrochloride. The ulnar artery was isolated above the wrist and doubly ligated with medium silk. A curved incision was then made over the palmar surface of the hand. The dissection disclosed the ulnar artery entering the tumor proximally and continuing in the superficial palmar arch, leaving it distally. The tumor was well circumscribed and easily removed. Bleeding was stopped by electrocoagulation, and the wound was closed with black silk sutures. The wound healed nicely, and the patient was discharged on April 4.

On May 29 he returned complaining of tenderness and pain in the operative region. A large fluctuant swelling was noted beneath the skinflap but not beneath the suture line. At the proximal end of this swelling there was a small, rather

hard, whitish nodule. The wrist was purple, and a long red streak was observed extending up the flexor surface of the forearm. Aspiration yielded a few drops of blood, but there was no free flow as before operation. Roentgen treatment was commenced, and the mass diminished in size. From June 1 to 6 the patient received 816 roentgens to the right hand. From June 30 to July 8 he received 1,067 roentgens to the right hand and 912 roentgens to the right axilla. There was only mild regression in the size of the tumor. On August 20 the tumor was noted to be three times its original size, and a large mass of hard glands was palpable in the right axilla. The entire hand and wrist were red. The patient died on September 3.

Description of Surgical Specimen.—Gross Description: The specimen consisted of a pear-shaped mass of tissue measuring 5 cm. in length and 3 cm. in diameter. Externally it was smooth and dark blue. From one pole a small artery protruded about 2 mm. At the other pole no distinct artery was seen, although there were a few tabs suggesting remnants of veins. On section the specimen was seen to

Fig. 2.—*A*, photographs of the hand before operation. *B*, photographs of the hand four months after operation, showing recurrence of the tumor. Note the red streaks extending up the forearm.

contain blood clot in various stages of organization; that near the center was friable, while more peripherally there were successive laminae of fibrous tissue and bood clot. The wall of this sac appeared to be continuous with that of the artery but was much thinned out. At one point in the center there were small radial streaks suggesting cholesterol crystals.

Microscopic Description: Section 1 was prepared and mounted on a large slide in order to show the entering artery. Only a short section of the artery was included, but this much appeared normal. The rest of the mass was composed of numerous endothelium-lined spaces of all sizes and shapes and containing red blood cells. Many of the spaces were linear, while others were cavernous or tortuous.

Section 2 showed a similar picture; the growth was fairly well encapsulated, and several apparently normal arteries of medium size lay on its outer margin. At some points encapsulation was less perfect than at others, but at no point could the vascular channels be traced outside of the main tumor mass. There were some areas which contained small cholesterol crystals. One gained the impression that there had been extensive hemorrhage followed by organization and hyalinization.

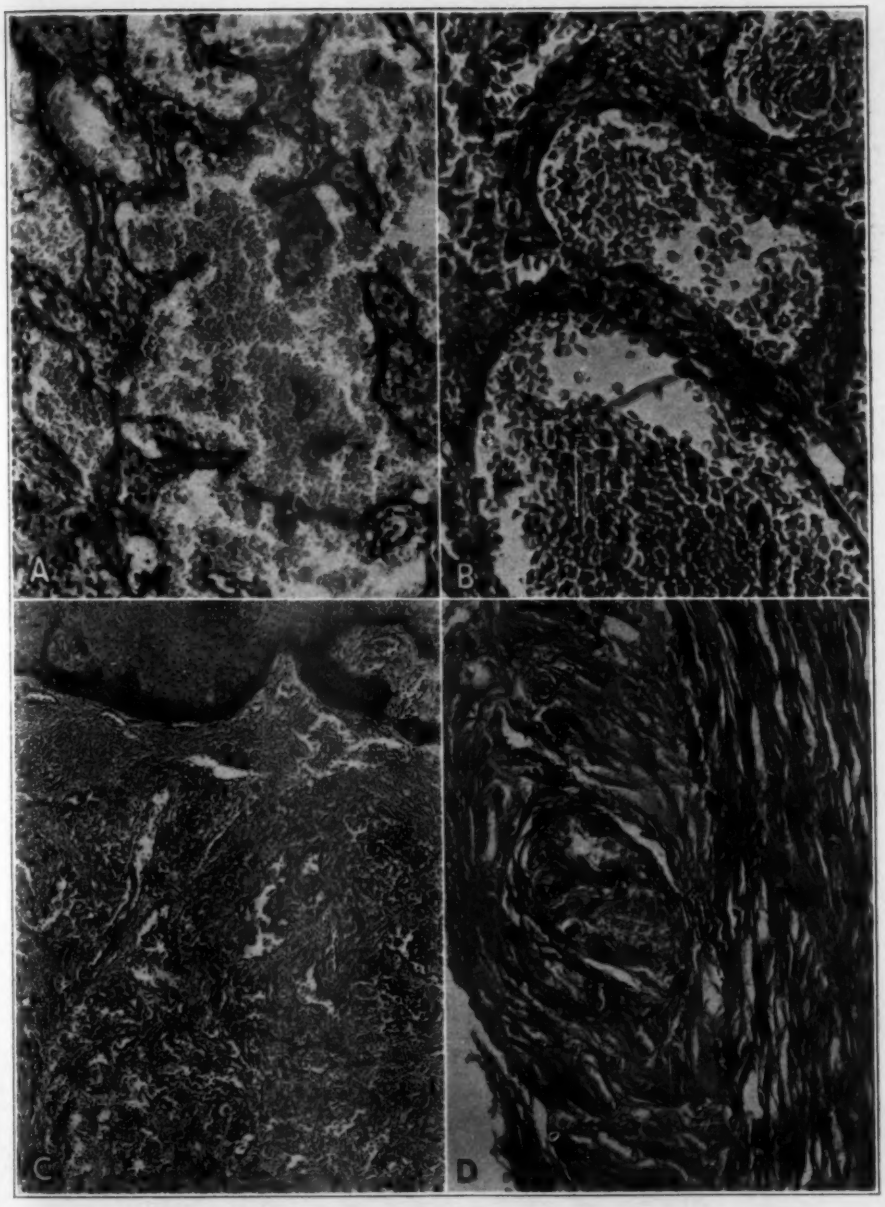

Fig. 3.—*A*, section of the original tumor showing the structure of a typical cavernous hemangioma. Hematoxylin and eosin; × 150. *B*, section from the recurrent tumor in the hand, showing the structure of a typical hemangioma. Hematoxylin and eosin; × 310. *C*, section of the recurrent tumor. Hyperplastic epithelium is shown in the upper part of the illustration, with the tumor directly beneath the skin. Hematoxylin and eosin; × 74. *D*, section from the epitrochlear node. There is complete replacement by the tumor, which here forms no vascular spaces. The cords of the tumor cells are lying at right angles to each other. Hematoxylin and eosin; × 150.

Verhoeff-Van Gieson's stain showed small areas in the periphery which contained reticulum. In no place, however, were these fibers really continuous enough to constitute even an aneurysmal wall.

Autopsy.—Autopsy was performed four hours after the patient's death.

Attached to the palmar surface of the right hand at its ulnar margin was a large hard tumor measuring 6 by 4 cm. It was adherent to the underlying structures, while the overlying skin showed a bluish discoloration extending up over the wrist for about 6 cm. After this mass was removed it was found to have eroded the fifth metacarpal bone, so that little of the osseous structure remained. On section the mass was seen to contain many spaces filled with blood, a good part of which had clotted; whitish areas or strands resembling fibrous tissue were also observed. The tumor did not seem to have a definite capsule except where it was attached to the skin. At this point a few muscles were adherent. On the flexor surface of the forearm, extending upward toward the elbow, was a fibrous band about 1 mm. in diameter. This lay directly beneath the skin and became more medial, until at the bend of the elbow it lay on the medial aspect and was attached to the firm epitrochlear gland. On section the gland was found to resemble the tumor below. Extending from the epitrochlear node upward to the axillary lymph nodes was another firm cord of the same type. The axillary nodes were considerably enlarged, measuring about 3 by 4 by 4 cm., and were apparently replaced by the same kind of tumor. These nodes were adherent to the axillary vessels and also to the ribs, but the tumor did not seem to have invaded the latter. There was no sign of intrapleural extension.

The heart weighed 550 Gm. There was marked coronary sclerosis. The chambers were dilated. Numerous small gray scars were seen in the myocardium.

The gallbladder contained twenty-five small cholesterol stones. At one point near the fundus the wall was thickened and firm, resembling a carcinoma. One firm node was found near the head of the pancreas.

The aorta was sclerotic and tortuous.

Other organs showed no significant changes.

Microscopic Notes: Sections from the hand showed the tumor to be covered by dense keratinizing epithelium, which was hyperplastic. Fresh hemorrhage, thrombotic material and polymorphonuclear leukocytes were widespread. The same blood spaces were seen as were found in the surgical specimen, but the lining cells were more dense and deeply staining. In places they were almost round. These had more oval nuclei, were vesicular and contained prominent nucleoli. Their cytoplasm was rather voluminous and did not tend to merge with that of the nearby cells. No definite mitotic figures were seen. There was no evidence of blood clot formation. In places the angiomatous structures showed active invasion of the surrounding tissues. A great deal of scarring and necrosis was evident. A section from the fifth metacarpal bone showed active destruction and fragmentation of the bone into small spicules.

The mass in the epitrochlear node showed bands of cells infiltrating between muscle bundles and replacement of the lymphoid tissue by tumor. However, there was no formation of blood spaces. The axillary nodes were almost completely replaced by tumor cells. Here there was a distinct tendency to the formation of vascular channels. The prussian blue reaction demonstrated a large amount of iron pigment. One of the large nerve trunks was completely surrounded and compressed by tumor.

The gallbladder and pancreatic node showed typical adenocarcinoma.

COMMENT

Recent reclassification [1e] of malignant vascular tumors has eliminated several of the older lesions formerly regarded as distinct entities. It is questionable whether the terms hemangio-endothelioma, perithelioma or perithelial angiosarcoma should be employed any longer. One may, however, recognize at least three fairly distinct groups: Kaposi's hemorrhagic sarcoma of the skin, primary angiosarcoma of the liver in infants and metastasizing hemangioma. Schlopsnies [3] in 1930 gave a fairly complete review of the reported cases of metastasizing hemangioma. Two subdivisions are convenient: those with a histologically benign structure (cases of Borrmann, Shennan and Ewing) and those with a histologically malignant structure (cases of Langhans and Wright). The case of Robinson and Castleman,[4] in which an apparently histologically benign primary tumor gave rise to histologically malignant metastases, appears to lie midway between these two groups or to form a connecting link. The case here reported seems to us to lie also in this class. It is evident that the formation of metastases is the deciding factor and not the histologic picture. The misleading diagnosis of "benign metastasizing hemangioma" should be discarded.

SUMMARY

A case of histologically benign hemangioma originating in or near the ulnar artery and clinically simulating an aneurysm is reported.

In spite of surgical removal and intensive irradiation, the tumor rapidly recurred and metastasized to the regional lymph nodes, exhibiting invasive and destructive features.

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3. Schlopsnies, W.: Ueber ein systematisiertes angioplastisches Sarkom in Milz, Leber und Knochenmark, Virchows Arch. f. path. Anat. **274**:85 (Nov.) 1929.

4. Robinson, J. M., and Castleman, B.: Benign Metastasizing Hemangioma, Ann. Surg. **104**:453 (Sept.) 1936.

A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Anomalies.—Geisinger [1] stated that supernumerary kidney has remained so rare that its discovery has been carefully recorded in most instances and has led to several diligent consultations of records. Thirty-eight cases of true supernumerary kidney, reasonably authenticated, are reported in the world's literature. To this number Geisinger added 2 cases, bringing the total to 40.

The accessory organ may be equal in size, and presumably in function, to its mate. In an occasional instance it has been larger; usually it is smaller and occupies a functional status equivalent to that of the ordinary hypoplastic kidney. Not infrequently the histologic detail may be considerably disordered; more generally it is comparable to that of the normal kidney. The vascular distribution varies to an extent that makes it profitless to attempt any description. The relationship of the associated ureters is more particular and more interesting and also of more practical consequence. Probably in a majority of cases the ureters become fused at some point, often near the bladder, so that only the usual two vesical orifices are present; in a number of cases, however, complete duplication exists, and either there are three orifices in the

1. Geisinger, J. F.: Supernumerary Kidney, J. Urol. **38**:331-356 (Oct.) 1937.

bladder or there is an extravesical orifice for the accessory ureter, located on the vulva, in the vagina, in the prostatic urethra or in a blind vesical or vaginal pouch.

Geisinger encountered considerable difficulty in making a satisfactory summary of the cases in his series, but the following facts are essentially correct: There were 27 cases in which the condition was discovered during life, 10 in which it was found at necropsy and 3 in which information of this nature was not given. The ureter was fused in 15 cases and not fused in 12 (ectopic in 3); it ended in a blind vesical sac in 1, was absent in 2 and was present but not traced or sufficiently described in 10, making a total of 40.

Amolsch [2] reported 4 cases of bilateral metanephric agenesia. Bilateral absence of kidneys is a rare and interesting anomaly. Unilateral absence, renal hypoplasia of some degree and various other gross malformations of the kidneys are encountered more frequently and present problems of practical importance in the field of urologic diagnosis. Bilateral renal agenesia is a condition incompatible with extra-uterine life. The fetus is frequently alive at birth, but death usually occurs within four hours, although Rosenbaum reported a case in which a child lived eleven days. The 4 cases presented by Amolsch bring the total of reported cases to 119.

It is difficult to establish a single causal factor which will explain fully all the recorded cases of renal agenesia. The reason for this exists in the fact that bilateral agenesia of the kidneys unaccompanied by some evidence of maldevelopment in other organs is essentially unknown. Almost invariably the urogenital system exhibits associated maldevelopment. The most common etiologic concept is concerned with abnormal pressure exerted during embryonic development. Explanation of renal agenesia rests on three possible errors of development; namely, the ureteral bud may fail to arise, the ureteral bud may appear but fail to reach nephrogenic tissue or the metanephrogenic cap may fail to develop.

Occurrence of renal agenesia has a definite predilection for the male sex. Sixty-three patients in the series of 119 were definitely identified as males and 24 as females, but 32 could not be classified because of grades of dysplasia rendering determination of sex impossible or because sufficient information was not supplied in the case report. The urinary bladder was present in 38 cases but was hypoplastic in 19; it was definitely absent in 35 cases. Ureters were identified in 2 cases in which the urinary bladder was absent, and in each the ureters terminated blindly at the caudal end and had slight bulbous enlargements at the cephalic end.

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2. Amolsch, A. L.: Bilateral Metanephric Agenesia, with a Report of Four Cases, J. Urol. **38**:360-370 (Oct.) 1937.

Sisk and Kundert [3] reported 2 cases of duplication of the lower part of the ureter with one ureter ending blindly. This condition is a developmental anomaly. There are two theories set forth to explain this type of duplication: premature or exaggerated cleavage of a single ureteral bud or the occurrence of duplicated ureteral buds arising from the wolffian duct.

Characteristic symptoms do not occur with this condition. In both of the cases reported in this paper hematuria was the important symptom. One patient suffered a mild degree of pain; the other experienced no pain.

Neither an excretory urogram nor the usual retrograde pyelo-ureterogram will reveal such ureters, except when the ureteral catheter enters the ureter which has the blind ending, as in the first case. When this occurs, a retrograde injection will, of course, show the ureter with the blind ending, and the normal pelvis will be shown by the excretory urogram. Use of the retrograde pyelo-ureterogram made with a large catheter or bulb just within the ureteral orifice is the method of choice and is most likely to reveal the condition.

Resection.—Goldstein and Abeshouse [4] reviewed the literature on resections of the kidney and collected reports of 290 cases in which this operation was performed and added reports of 6 personal cases.

Partial resection of a kidney is the operation of choice in the treatment of the following localized diseases of the kidney: solitary serous or hemorrhagic cysts; hydatid cysts; localized hydronephrosis or pyonephrosis, with or without renal calculi; benign tumors; localized cortical abscesses; renal carbuncles; renal infarct, and renal fistula. Partial resection of a kidney is contraindicated in the treatment of tuberculosis or malignant tumors of the kidney in the presence of a healthy kidney on the opposite side. Partial resection is occasionally indicated in the treatment of extensive bilateral disease, such as tuberculosis, calculous pyonephrosis and rupture of the kidney. Under such circumstances, it becomes an operation of necessity.

In operations requiring extensive reduction of the total kidney substance (the removal of one kidney and from a half to a third of the other kidney or bilateral resections) it is advisable to perform the operations in two stages with an interval of at least four to eight weeks between operations. The minimal amount of renal substance necessary to maintain life in man is one fourth of the total renal substance (one half of one kidney).

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3. Sisk, I. R., and Kundert, Palmer: Duplication of the Lower Ureter Ending Blindly, J. Urol. **38**: 261-266 (Sept.) 1937.

4. Goldstein, A. E., and Abeshouse, B. S.: Partial Resections of the Kidney: A Report of Six Cases and a Review of the Literature, J. Urol. **38**:15-42 (July) 1937.

Successful partial resection demands an orderly plan of operation, which includes proper surgical approach, preparation of the vascular pedicle and ligation of the nutrient vessels to the segment to be removed, decapsulation of the kidney in the operative area and utilization of this portion of the capsule in closing the wound, incision through healthy tissue and accurate hemostasis and approximation of the wound.

Hess [5] discussed the indications for and the limitations of heminephrectomy. He observed 17 cases of horseshoe and unilateral fused kidney, in 6 of which definite surgical intervention was necessary, heminephrectomy being done in 4. There were over 100 cases of unilateral or bilateral double kidney, in 9 of which surgical intervention was necessary. Heminephrectomy was performed in 8 of these cases; in 1 case it was done for tuberculosis, in 1 for incontinence due to an ectopic ureter from the upper half of the ureter opening into the female urethra and in the remaining cases for hydronephrosis, pyonephrosis or calculus or for some combination of these diseases, when the condition was diagnosed as being limited to one segment. There were 11 cases of anatomically normal kidneys in which partial nephrectomy was done. In 5, total nephrectomy was done on one kidney and heminephrectomy on the remaining kidney, the indication being bilateral calculous pyonephrosis and hydronephrosis. Heminephrectomy was performed in 5 cases of calculous disease, in 3 of which the disease was limited to the upper pole and in 2 of which it was limited to the lower pole with mild infection, and in 1 case of pyonephrosis in which the infection was limited to the lower pole of the kidney and complicated by a perirenal inflammatory process.

In all cases of horseshoe kidney in which heminephrectomy was performed the approach was through the usual lumbar retroperitoneal exposure. It is advisable wherever possible to sever the isthmus with the actual cautery or with the radio knife. It is also advisable whenever possible to ligate and divide those vessels which go to the isthmus. This frees the remaining half and allows it to assume a more nearly normal position. In removing half of a horseshoe kidney it is essential to attempt to free the ureter sufficiently to insure adequate drainage from the segment saved.

Usually there is a distinct blood supply to both portions of a double kidney. Careful dissection of the pedicle will enable the operator before attempting heminephrectomy to ligate the vessels which supply the segment that is to be removed. This simplifies the surgical technic, as amputation may be made in a distinctly nonvascular line of cleavage and hemostasis can be accomplished again by merely tying capsular flaps (natural ribbon sutures) over a pad of fat or muscle covering the raw surface.

5. Hess, Elmer: Heminephrectomy: Its Indications and Limitations, J. Urol. **38**:43-57 (July) 1937.

In removing segments of anatomically normally formed kidneys, if an aberrant vessel is found one may clamp it off, accomplishing much the same purpose as when one is dealing with a double kidney; however, it is often necessary to amputate the segment to be removed without ligating the vessels supplying blood to the segment.

In the author's series of cases there was no immediate mortality. One of the patients on whom heminephrectomy was performed for horseshoe kidney died of metastasis a little over a year after operation. In another case calculous nephrosis developed in the remaining half of the kidney, but the patient was living twelve years after the primary heminephrectomy. There were no deaths following any operations on double kidneys or on anatomically normally formed kidneys. All of the patients were reexamined, and at the time Hess' report was written they were comparatively free from the symptoms which brought them to the clinic.

Hydronephrosis.—Smagghe [6] discussed the opinions expressed by various operators in regard to the treatment of hydronephrosis. He reported 12 cases and stated that bilateral hydronephrosis is comparatively common. The frequency of this condition is brought out by more universal use of intravenous pyelography. Infection and calculi are seen frequently in association with hydronephrosis and are due to stasis of the urine and alteration in the urinary acidity.

Radical treatment was carried out only when the opposite side proved to be normal. Drainage of one kidney is advisable in some cases of hydronephroses when extensive involvement of the opposite side makes conservative treatment necessary.

Pilcher [7] reported a case of bilateral congenital hydronephrosis in a woman aged 38 which demonstrated several points of importance in the conservative treatment of this condition.

On the left side large anomalous vessels which could not be severed were found running to the lower pole. The pelvis was resected, and the ureter was reimplanted anteriorly to the vessels. On the right side a definite ureteral stricture was found extending below the ureteropelvic junction. The pelvis and the strictured area of the ureter were resected, and the ureter was reimplanted in the remaining portion of the pelvis. In both instances a nephrostomy tube was inserted, and a soft rubber catheter was passed through the lower calix and down into the upper portion of the ureter. This catheter, used as a ureteral splint, was removed ten days after the operation. Subsequently, on each side, it was found that when the nephrostomy tube was clamped the patient

6. Smagghe, H.: Les hydronéphroses bilatérales, J. d'urol. **43**:5-33 (Jan.) 1937.

7. Pilcher, Frederick, Jr.: The Treatment of Bilateral Congenital Hydronephrosis, Proc. Staff Meet., Mayo Clin. **12**:279-282 (May 5) 1937.

experienced pain and that drainage from the kidney was inadequate. A ureteral catheter passed upward from the bladder on the left side was allowed to remain in place several days, improving the drainage on this side. It was, however, necessary to operate on the right side a second time. This time a ureteral splint was left in place approximately three months, and when it was removed drainage from this kidney was entirely adequate. Cabot [8] emphasized the importance of maintaining the catheter in position for a prolonged period of time in order to avoid contraction of scar tissue in this region, with resultant obstruction. He stated that two or even three months is the proper time to leave such a splint in place.

Vermooten [9] stated that the South African Negro (Bantu) does not experience the formation of renal calculi, as illustrated by examination of the records of 1,091,000 Negroes admitted to the Johannesburg General Hospital. Members of the white population of South Africa, as illustrated by examination of records of 126,000 white patients admitted to this hospital, have renal calculi in the ratio of 1 to 460 patients. The South African Negro lives on a simple, stable and uniform diet, which is rich in vitamin A, has an acid ash base and is extremely low in content of calcium. Urinary stasis and infection play an important part in the formation of renal calculi. The efficacy of administration of vitamin A should regularly be checked by studying regeneration of the visual purple, so that one can be certain that it is available for assimilation.

Marion [10] discussed a condition under the term *ensablement*. Roentgenograms of patients with this condition reveal the apparent presence of a large coraliform stone in the kidney or blockading the ureter, which on operation proves to be not a stone but a large mass of gravel, completely opaque to roentgen rays, filling large portions of the renal pelvis and even the excretory tubules of the kidney.

Masses of this kind may produce complications as great as those caused by true calculi. Marion expressed the belief that certain postoperative anurias are due to obliterations of the renal tubules by minute crystals which patients sometimes eliminate in great quantities after certain operations, particularly those on the urinary tract.

The filling of the ureter with gravel is a painful experience for the patient after elimination of a great amount of gravel at one time. Moderate amounts of gravel may be eliminated without the patient's knowl-

8. Cabot, Hugh, in discussion on Pilcher,[7] pp. 282-283.

9. Vermooten, Vincent: The Occurrence of Renal Calculi and Their Possible Relation to Diet as Illustrated in the South African Negro, J. A. M. A. **109**:857-859 (Sept. 11) 1937.

10. Marion, G.: De l'ensablement du bassinet ou de l'uretère, J. d'urol. **43**: 297-303 (April) 1937.

edge if there are two well functioning kidneys. But when only one kidney is working and the ureter becomes clogged with gravel to the point of complete obstruction, the result is anuria accompanied by severe renal colic.

The same results follow if the renal pelvis and the calices become similarly packed with gravel or what may be called a mud pack. It can be readily understood that under the influence of a water cure or of certain diuretic medicaments this clogging may be resolved by the gradual elimination of the gravel. This occurred in the case of a young girl whose roentgenograms, taken eight months apart, showed in the first what appeared to be a large coraliform stone and in the second a calculus only the size of a small bean. This patient reported that two or three months previous to the second roentgen examination she had experienced a severe attack of renal colic, followed by spontaneous elimination of a large amount of urinary gravel. Thus it was evident that the supposed coraliform stone had not been a stone but was a large mass of gravel.

Cases of this kind are not frequent and appear to be rather little known to urologists. Much more common are cases in which true lithiasis is accompanied by masses of gravel within pyonephritic pockets.

Raising the question whether one can recognize these masses in the roentgenogram, Marion stated that it is not always possible. If an entire ureter appears opaque, one may think of such a condition; but more frequently this is not the case, and gravel is not considered. If gravel is in the renal pelvis and the contour is a little indistinct, not so sharp or so well defined as that of a calculus, one may likewise suspect such a condition. In two roentgenograms the images indicated something less compact than a stone, which might well orient the diagnosis in the right direction. But unless this is the case, it is impossible to foresee the existence of an agglomeration of gravel in advance of operation. However, this is not of capital importance, for if there is anuria, whatever the cause, ureteral catheterization without delay is the proper recourse, and this will usually open the ureter blocked with gravel. If, on the other hand, the pelvis is packed with gravel that resembles a calculus, the indication for operation is absolute, no matter whether gravel or a true calculus is present.

Discovery of the etiology of urinary calculus is essentially a urologic problem. For the past seven years Randall and Melvin [11] have been interested especially in the problem of the etiology of primary renal calculi and have repeated in experimental studies, in one form or another, most of the conditions theoretically productive of stone. They have a firm conviction that there has to be an initiating lesion in the

11. Randall, Alexander, and Melvin, P. D.: The Morphogeny of Renal Calculus, J. Urol. **37**:737-745 (June) 1937.

formation of primary renal calculus. According to them, everything points to it, every fact strongly suggests it, every pertinent question demands it and the pathologic picture itself is incomplete without it. Stone is a symptom and not a disease entity. Stone is made from the common salts in the urine and may be formed of any one of such salts or of any combination of these salts. A stone will form on any foreign tissue or foreign body and is a gradual accretion of crystals demanding a nidus for the seeding of such crystallization. The formation of a stone requires time, and the stone must be stationary for a given period in order to gain clinical size. Randall and Melvin therefore created a primary postulate; that is, that there must be an initiating lesion which precedes formation of a renal calculus.

In the postmortem examination of a large series of kidneys Randall and Melvin opened the pelvis first, then carefully inspected each major and minor calix and examined each renal papilla with a hand lens. It was tedious work, but they were not long in finding a most interesting pathologic lesion. To date 298 pairs of kidneys have been examined. Twenty-eight of these have shown a macroscopic lesion of the renal papilla heretofore unrecognized. The lesion consists of a deposit of calcium in the walls of the renal papillae. In 11 instances such a deposit was found in both kidneys, while in 4 cases it occurred in only one of a pair of kidneys. In a few instances only one papilla presented a macroscopic calcium plaque, though generally more than one, but not all papillae would have a variable amount visible. In 8 instances actual stone was found in the act of crystallizing on such a calcium plaque and still firmly adherent to the same. Multiple variations of this picture have been observed. The plaques were subjected to microscopic section and specific staining in order to identify the chemical composition, and, further, enough material was teased out for direct chemical analysis. By these means it was proved satisfactorily that the plaques were composed of calcium.

Two clinical observations which have been made repeatedly have long held the authors' attention. The first is the frequency with which the smallest shadows of renal calculi are to be found in the position of the minor calices and are likewise multiple in a given kidney. Good roentgenograms and good urograms have substantiated the observation over and over again. The second is the fact, demonstrated by magnification of small calculi, especially those that have been passed rapidly or have been promptly removed, that while the greater part of the surface of such small calculi is highly crystalline, there is almost uniformly one surface which is smooth, slightly depressed and distinctly different from the remainder. This surface gives every suggestion to the eye that it has been a point of mural attachment and is now considered to be such.

Microscopic sections have been made through the plaques of calcium in the walls of the renal papillae. Study of these sections has shown that the first deposit is regularly within the papilla and not on its surface. It is not the familiar intratubular cast but spreads out through the interstitial tissue as a definite morbid process and deposit. The most important fact to be observed is that this primary calcium deposit is definitely beneath the surface and is noninflammatory.

There is evidence that as such a calcium plaque increases in size the covering epithelium loses its support and nutrition, and the plaque is denuded gradually of the epithelial tissue covering it.

One kidney gave evidence of three papillae with the simple calcium deposit, but on a fourth papilla there was a characteristic crystalline calculus growing directly on a calcium plaque. This calculus was approximately 2 by 3 mm. in size, of brownish tint and firmly attached.

An important fact is again pointed out: In none of the foregoing cases was there the slightest evidence of an infection or of an infectious process, contrary to generally accepted opinion; this holds true for numerous slides of similar lesions that have been subjected to microscopic study.

Tuberculosis.—Klasson [12] compared a series of 42 cases of renal tuberculosis in children under 16 years of age observed by Wildbolz with a series of cases of tuberculosis in adults. He concluded that the disease is fairly common in children. In the first ten years of life it is found rarely but increases in frequency rapidly after this time, until, at the end of the second decade of life, it is as common as in the third decade. Bilateral renal tuberculosis is found twice as often in children as in adults, but its origin, as in adults, is apparently unilateral in most instances.

The pathologic process in children is similar to that occurring in adults. Although genital tuberculosis in male children is less frequently seen in association with tuberculosis of the urinary tract than it is in later periods of life, in the majority of children having tuberculosis of the urinary tract tuberculous foci are also found in other organs, such as the lungs and bones. The symptoms, treatment and prognosis are the same in children and adults.

Tumors.—Mathé [13] expressed the belief that nephrectomy is still the treatment of choice in cases of carcinoma of the kidney. Irradiation is of value but should not supplant surgical removal. Preoperative irradiation is of value in producing regression of huge growths, thereby rendering certain inoperable tumors operable. Postoperative irradiation

12. Klasson: Ueber die Nierentuberkulose bei Kindern, Ztschr. f. urol. Chir. u. Gynäk. **43**:194-201, 1937.

13. Mathé, C. P.: Cancer of the Kidney: Present-Day Status of Its Treatment and End-Results, California & West. Med. **46**:385-390 (June) 1937.

is employed to lessen the risk of metastasis. Irradiation of inoperable tumors, although of some palliative value, has not effected permanent relief.

Hematuria is the most constant and outstanding symptom, and the attending physician should bear in mind cancer of the kidney when attempting to make a differential diagnosis for patients suffering from hematuria.

Success following surgical excision depends on the employment of certain surgical technic consisting of early ligation of the renal pedicle, sufficient exposure of the field of operation, a minimum amount of trauma, gentle manipulation and postoperative irradiation.

In the series of cases reported by Mathé, 10 of 24 patients treated by nephrectomy (12 of whom also received postoperative irradiation) were living and well from two to fourteen years after operation (eight five year cures) and 3 were relieved by partial resection. Thirteen of the 27 patients operated on (44 per cent) apparently were relieved, 33.3 per cent of the cures being of five years' duration, demonstrating that surgical removal supplemented by irradiation is the treatment of choice and is more likely to be followed by a cure.

Mintz [14] reviewed 93 cases of sarcoma of the kidney in adults. Nine were found among the records of the Massachusetts General Hospital, 2 were private cases and the remainder were reported in the literature.

The age was not stated in 21 cases. Forty, or 55 per cent, occurred in persons between 40 and 60 years of age. Twenty-three of the patients, or 33 per cent, were less than 40 years of age, while only 9, or 12 per cent, were in the sixth and seventh decades.

The histopathologic structure of these tumors is quite varied and for all practical purposes is of little help. They all seem to be equally effective in producing the same end-result, that is, death. In the group of cases reviewed by Mintz there were 23 spindle cell sarcomas, 12 fibrosarcomas, 16 sarcomas, 6 leiomyosarcomas, 4 mixed cell sarcomas, 2 Wilms' tumors, 11 embryonal mixed tumors, 2 embryonal myosarcomas and 1 each of several other types.

The symptomatology is not unlike that accompanying other types of cortical tumors in adults. The tumor mass is not as predominant a symptom as in sarcoma in children. The triad of hematuria, tumor and pain is the chief complaint. Symptoms of a gastro-intestinal nature, such as nausea, vomiting, eructations and constipation, appear to be slightly more frequent than in other forms of renal neoplasm.

Of the 78 patients on whom nephrectomy was performed, no follow-up study was made on 23. Thirty died, 19 of these postopera-

14. Mintz, E. R.: Sarcoma of the Kidney in Adults, Ann. Surg. **105**:521-538 (April) 1937.

tively. The causes usually given were shock and hemorrhage. At the time the author's report was written, 21 patients were living, 15 for less than one year. Six had passed the first year, 3 of whom had lived beyond the five year period. Of these 3, 1 had lived twenty years, but the histologic diagnosis of sarcoma seemed to be in doubt. Five patients underwent an exploratory laparotomy. Of these, 2 died postoperatively, and necropsy revealed evidence of multiple metastases. The condition in 3 was found to be inoperable.

Caulk [15] stated that with few exceptions tumors of the renal pelvis are epithelial, the majority being of the papillary variety. According to authorities, papillary tumors constitute about three fourths of the growths in the renal pelvis.

Papillary tumors have a tendency to be multiple and occur more frequently in men than in women. On the other hand, squamous cell and other invasive tumors occur in about the same proportion in men as in women. The papillary tumor possesses the notorious quality of involving other parts of the urinary system, particularly the ureter and the bladder on the corresponding side and occasionally the opposite ureter, either simultaneously or with recurrences. This occurred in 50 per cent of cases. The infiltrative squamous growth lacks this trait. This decided difference has a definite bearing on the type of surgical procedure. After removal of a kidney for pelvic tumor, a gross pathologic examination should be made, and in case the tumor is papillary, nephroureterectomy with partial resection of the bladder is necessary, otherwise nephrectomy will suffice.

The papillary tumor is slow in progress and is not nearly as malignant as the nonpapillary tumor. It is seldom associated with any preexisting pathologic factors, such as stone or leukoplakia, whereas the nonpapillary growth is decidedly malignant and occasionally is associated with stone, infection or leukoplakia. As a rule, the associated tumors are similar in their histologic structure to the neoplasm of the pelvis.

The diagnosis of pelvic tumor is made chiefly by urographic study. The majority of tumors are associated with profuse hematuria; rarely is there a palpable renal tumor, except in instances of hydronephrosis or hematonephrosis. Renal pain has been common in all cases reported and usually results from pelvic block, with resulting pyelectasis. Urographic evidences of filling defects in the pelvis and ureter may again be deceptive and may not represent neoplasm. Intravenous urography may be of assistance to the diagnostician in certain cases, but delineation

15. Caulk, J. R.: Tumors of the Renal Pelvis and Ureter, Ann. Surg. **106**:68-84 (July) 1937.

by this means is seldom as cleancut as by retrograde pyelography. In 2 of the cases in Caulk's series in which retrograde pyelography was impossible on account of ureteral block, no dye was excreted to give the necessary information.

Treatment of tumors of the renal pelvis is surgical and varies with the type of tumor. As in the case of all tumors, early diagnosis is most essential for the future welfare of the patient. Unfortunately, because hematuria is painless, the patients are not seen in the early stages of the disease, and in cases of invasive squamous cell tumor the majority of the growths have extended beyond the hope of cure. The regional lymph nodes are often involved; hence the prognosis is poor. Simple nephrectomy is usually all that is necessary, since these tumors possess little tendency to involve the ureter.

In the group of papillary tumors, benign and malignant, more than nephrectomy is required, although this is the operation which has been performed initially in the majority of instances.

Caulk, in his article, quoted from one published by Kimball and Ferris,[16] who reported 74 cases of such tumors which involved more than one portion of the urinary tract. Forty of the patients were treated by nephrectomy and 25 by nephro-ureterectomy which did not include the intramural part of the ureter. Of the 40 patients treated by nephrectomy, 30, or 75 per cent, had recurrences; 21 of these required a secondary ureterectomy, with further recurrence in 12, or 57 per cent. The known mortality in the group treated by nephrectomy was 33 per cent. Primary nephro-ureterectomy which did not include the intramural part of the ureter was performed in 25 cases; there were known recurrences in 17, or 68 per cent. Further resection of the intramural portion of the ureter was effected in 12 cases, with further recurrences in 4. The known mortality for this group was 44 per cent. Only 6 patients were treated by primary nephro-ureterectomy which included the intramural part of the ureter. Two had tumors that were diagnosed as benign and 4, tumors that were considered malignant. The known mortality in the group with malignant tumors was 25 per cent. Both patients with benign tumors were living at the end of eleven years. In the entire group of 74 patients 28 were known to be dead—a mortality of 38 per cent. Since 33 per cent of the patients in this series had tumors in the ureter and bladder as well as in the kidney at the time they consulted a urologist and since 86 per cent of all the recurrences appeared in the remaining ureteral stump and ureteral orifices,

16. Kimball, F. N., and Ferris, H. W.: Papillomatous Tumor of the Pelvis Associated with Similar Tumors of the Ureter and Bladder, J. Urol. **31**:257-304 (March) 1934.

Kimball and Ferris stated that a method of treatment should be chosen which would remove the disease in its entirety.

Several technics have been proposed; the most favored at present and the one which to Caulk is unquestionably the most satisfactory is nephro-ureterectomy by a combined lumbar and lower midline exposure.

Priestley [17] stated that primary squamous cell tumors of the renal pelvis are of two types, papillary and nonpapillary. Both are relatively uncommon, the nonpapillary variety being quite rare. Differentiation of these two types of tumors is of importance because they differ clinically, pathologically, prognostically and in the procedure of choice best adapted for their surgical approach. The papillary tumor is usually lower in grade of malignancy, runs a slower clinical course and metastasizes by implantation into the ureter and the bladder. Generally speaking, if not too far advanced, this growth offers a reasonably good prognosis when treated by nephro-ureterectomy with removal of the adjacent bladder. On the other hand, the nonpapillary variety tends more often to run a rapidly fatal course. Pathologically, such a growth appears of a higher grade of malignancy. The growth occurs by extension into the kidney and its surrounding structures and by the occurrence of distant metastasis. Nephrectomy, with removal of a relatively short portion of the adjacent ureter, suffices, since metastasis does not occur by distant implantation in the ureter and bladder. Postoperative longevity seldom has exceeded nine months.

Renal Operations.—Goldstein [18] reported a series of 43 (12.5 per cent) accidents occurring in 345 operations on the kidney. Eight patients (20 per cent) died, 4 from hemorrhage. Hemorrhage was responsible for 49 per cent of the serious accidents. Nine kidneys were sacrificed because of uncontrollable hemorrhage, but in these instances there were no deaths. In 3 patients bleeding came from the injured aberrant vessels; in 2, from injured retropelvic vessels, and in 4, from the kidney proper. Goldstein stated that all bleeding should be controlled before the patient leaves the operating table. Clamps should be left on the pedicle without hesitation when necessary. The clamps should be placed with great care. Opening of the diaphragm, the pleura or the peritoneum is not a serious accident. If possible, such rents should be closed, but the renal bed should be drained. Opening of any part of the intestinal tract is a serious accident, and closure should be done immediately. Fracture of a rib or division of a nerve is not a serious accident; nature will take care of such injuries.

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17. Priestley, J. B.: Non-Papillary Squamous Cell Epithelioma of the Renal Pelvis, J. Urol. **37**:674-679 (May) 1937.

18. Goldstein, A. E.: Accidents in Renal Surgery, Surg., Gynec. & Obst. **65**: 515-522 (Oct.) 1937.

Function.—Schulhof [19] reported the effect of surgical drainage on functionless kidneys. In 260 cases in which surgical drainage was performed on the kidney for conditions other than lithiasis, 40 of the operations were performed on apparently functionless kidneys. Of this group, 10 cases were selected because relatively complete studies were carried out which appeared to authorize drawing of conclusions. The 10 cases were divided into two groups: 6 cases in which complete preoperative and postoperative studies were made and 4 cases in which intravenous urography alone was used as a test of differential function.

In these 10 cases, 4 of the patients were women and 6 were men. The average age at the time of operation was 38 years, the youngest patient being 9 years of age and the oldest 52. The average age at the onset of symptoms was 35 years.

In 9 cases there was pus in the urine. Positive cultures were obtained in 6 cases, Escherichia coli being the predominating organism. In 4 cases in which Esch. coli had been demonstrated before the operation, it could not be cultured from the postoperative specimens. The value for blood urea was normal in 8 cases before operation and abnormal in 2 cases. In 8 cases the left kidney was involved, and in 2, the right kidney. In 8 cases nephrostomy was performed, while in the 2 remaining cutaneous ureterostomy was resorted to. In 5 cases in which both dye tests and intravenous urography were employed to ascertain differential renal function, there was close agreement between the two concerning the state of renal efficiency. In most cases the period of time which elapsed between the operation and the postoperative tests of renal function was about twenty days.

Definite improvement was noted in renal function in each of the 10 cases as a result of surgical drainage. In 4 cases the drained kidney functioned as well as the opposite kidney; in 5 cases function returned to approximately 50 per cent of that of the other side, and in 1 case, function returned to the extent that good visualization was delayed until a urogram was made sixty minutes after the intravenous injection of the contrast medium.

Pilcher, Bollman and Mann [20] studied the effect of increased intraureteral pressure on the renal function of trained dogs under nearly normal physiologic conditions. The kidney on one side was made to secrete against definite pressures for periods too short to injure the organ permanently, and the quantity and composition of the urine thus

19. Schulhof, M. G.: The Effect of Surgical Drainage on Kidneys Declared Functionless by Present Tests of Renal Function, Surg., Gynec. & Obst. **65**:188-194 (Aug.) 1937.

20. Pilcher, Frederick, Jr.; Bollman, J. L., and Mann, F. C.: The Effect of Increased Intra-Ureteral Pressure on Renal Function, J. Urol. **38**:202-211 (Aug.) 1937.

secreted was compared with that of the urine secreted from the opposite kidney, which was under normal conditions of pressure.

The results of this study indicate that the kidney will secrete urine that is normal in quantity and composition against pressures up to and including one of 30 cm. of water. At pressures of 40, 50 and 60 cm. of water there is a regular diminution in the volume of urine and often a greater diminution in the total amount of chloride. There is no change in the total amount of creatinine and urea at pressures less than 60 cm. At a pressure of 60 cm., a slight diminution in the total amount of creatinine and urea begins to occur. The excretion of phenolsulfonphthalein is first diminished at a pressure of 35 cm., and a progressively decreasing output occurs as the pressure is increased.

Causing the kidney to secrete against pressures up to and including 60 cm. of water for one hour did not affect the function of the opposite kidney, nor was a significant anuria or polyuria of either kidney ever observed.

In those instances in which unilateral infection of the kidney occurred, the infected organ excreted the larger quantity of urine and chloride, whereas the healthy kidney excreted almost the entire quantity of creatinine, urea and phenolsulfonphthalein.

Hortolomei, Burghele and Streja [21] stated that it is now assumed universally that the upper part of the urinary tract must be considered as a complex apparatus, assuring evacuation by its functioning, and not, as was formerly believed, just a tubular system through which the urine flows toward the bladder. The present day knowledge with reference to innervation of the organs of the vegetative nervous system enables one to affirm that the tonicity of the urinary tract is maintained by the sympathetic nervous system and its motor functions are maintained by the parasympathetic nervous system.

The modern notion of the functional unity of the ureter has been arrived at by clinical observation, aided by intravenous urography. The urinary tract, both topographically and functionally, is divided into two portions, one portion being devoted to the transportation of the urine (pyelo-ureteral tract) and the other to its collection in a reservoir (bladder) with a draining canal (urethra). The upper part, which is the active part of the urinary apparatus, must continually adapt itself to the work it has to do. The functional modifications that have this end in view are uniformly the same throughout the entire length of the conduit, from one end of the excretory tract to the other. In a normal conduit they are never localized predominantly or exclusively in one segment.

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21. Hortolomei, N.; Burghele, T., and Streja, M.: Considérations sur la physiopathologie des voies urinaires supérieures, J. d'urol. **43**:399-429 (May) 1937.

Similarly, in cases of pathologic involvement reaction of the organ is the result of an exaggeration of the physiologic methods of functional overactivity, and this too will be general. From the pathologic point of view there is only one division that counts, namely, that which is determined by the site of the lesion.

Those authors who have studied the variations of intrapyelo-ureteral pressure have recognized that the internal pressure varies with peristalsis and progressively increases from the pelvis to the juxtavesical portion. Similarly, the intra-ureteral pressure is always greater than the intravesical. This difference is maintained even when the bladder is under tension, for vesical repletion causes intra-ureteral pressure to increase in a line parallel with it.

Functional interactions exist between the kidneys and their excretory apparatus, the purpose of which is to maintain functional equilibrium within the urinary apparatus.

One of the most interesting aspects of the problem of functional relations between the gland and its excretory apparatus is the influence of diuresis on the functioning of the urinary tract. Experimental research has shown that adaptation of the upper part of the tract to an increase in diuresis is brought about progressively, the quantity of urine becoming greater and greater and the frequency of peristalsis increasing, until at length a limit is reached in fatigability of the muscle fibers. At this point the only means of adaptation to the quantity of urine to be evacuated is an increase of the amount transported by each wave. This becomes possible only through dilatation of the canal, which is produced by lowering the tonicity of the latter. Thus, adaptation of the canal to an increase in diuresis is made first by a physiologic hyperkinesia and second by a physiologic hypotonia. This has also been confirmed by intravenous urography.

Relations between the upper part of the urinary tract and the bladder are so close that every physiologic modification or pathologic change of the one has a repercussion on the other. One of the most recent discoveries has been that the state of repletion or of vacuity of the bladder has a definite effect on the upper part of the urinary tract. The same forces of hypotonia and hyperkinesia are plainly at work here.

The question recently arising as to whether there exists normally at the level of the upper part of the urinary tract portions which constantly contain urine has apparently been settled in the negative. Another question still remains open; that is, whether there are sphincters existing along the upper part of the urinary tract, dividing the tract into segments, such as some authors have described. The presence of a peripapillary sphincter is probably illusory, but the question of subpyelic sphincters is not so simple. No one has ever demonstrated these histologically,

and yet their functional existence is beyond dispute if the pelvis is watched emptying itself under the fluoroscopic screen.

When diuresis increases, the tone of the excretory canal is lowered. But if one assumes that this physiologic hypotonia is unequal, or that its effects are unequal at different points of the canal, all is easily explained. The most tonic portion lets the wave pass only at the moment of systole, when the force of propulsion from the pelvis overcomes its tone. Evacuation occurs at that moment in the manner described by Legueu, who observed it by means of the pyeloscope. When diuresis again becomes moderate, the pyelic tone returns to its normal level, and presently there is nothing to differentiate functionally the pelvis and the ureter from "these sphincteral regions."

Hormonal influences appear to exert some action on the functioning of the upper part of the urinary tract, especially the influence of the hypophysis. To accomplish normal functioning of the urinary apparatus, two conditions are necessary: (1) functional integrity of its dynamic elements and (2) anatomic integrity of the pathways of evacuation, assuring a free outlet for urine. The commonest dynamic disturbances from exaggeration of function are hypertonia and hyperkinesia, which provoke colic. That patients with such a disturbance of function suffer with a local neurovegetative disequilibrium has been recognized, especially in America, where cure has been effected by suitable neurologic treatment.

On the other hand, there are dynamic difficulties owing to diminution of function, better known as hypotonia, hypokinesia and atony. Primary hypotonia results most commonly from infection, and from the start it paralyzes or diminishes the capacity of the conduit for reaction to its disturbances with respect to urinary evacuation. Some of these cases are of endocrine origin and some are congenital.

Whenever a primary hypotonia of dynamism accompanies or precedes a disturbance provoked by a mechanical obstacle, urinary stasis is more marked than it would be if either factor were present alone. Examples of this are found in uterine pressure, which aggravates the hypotonia of pregnancy, and in infection, which increases stasis in the presence of ureteral calculi.

Renal Osteitis Fibrosa.—Albright, Drake and Sulkowitch [22] reported a case of a condition termed "renal osteitis fibrosa generalisata" and included the results of postmortem examination. Two similar cases are cited. The characteristics of the disease are long-standing severe renal insufficiency, marked retention of phosphate, a normal or low level of serum calcium, severe acidosis, arteriosclerosis, calcium deposits

22. Albright, Fuller; Drake, T. G., and Sulkowitch, H. W.: Renal Osteitis Fibrosa Cystica: Report of a Case with Discussion of Metabolic Aspects, Bull. Johns Hopkins Hosp. **60**:377-399 (June) 1937.

around the joints and extreme enlargement of all parathyroid glands. The histologic changes in the bone in this disease are indistinguishable from those seen in primary hyperparathyroidism. Hyperplasia of the parathyroid glands is thought to be compensatory, owing to the retention of phosphates.

Metabolic studies of the patient while on a diet low in calcium showed increased excretion of calcium and phosphorus in the feces, slightly decreased or even normal excretions in the urine and only slightly increased total excretion of calcium and phosphorus as compared with that of normal persons.

In the differential diagnosis between primary hyperparathyroidism leading to diseases of the bone and kidneys and disease of the kidneys leading to compensatory hyperplasia of the parathyroid glands and diseases of the bone, the following points are stressed: 1. The presence of a tumor in only the parathyroid glands shows that the disease most certainly started there. 2. The fact that the first symptoms are renal rather than skeletal does not prove that the disease originated in the kidneys, because many patients who have primary hyperparathyroidism complain only of renal symptoms and never complain of skeletal symptoms. 3. The level of serum calcium should be high in primary hyperparathyroidism and normal or low in disease which originates in the kidneys.

Cysts.—Tenenbaum [23] reported a case of renal echinococcus cyst in which there occurred obscure preoperative syndromes and a grave postoperative reaction. Early diagnosis is important to guard against the possibility of grave complications arising from infection and rupture of an unrecognized cyst. Of equal importance is the choice of the proper operative procedure: aspiration of half the contents of the sac, followed by the injection of a 10 per cent dilution of solution of formaldehyde, U. S. P., or absolute alcohol, marsupialization of the sac or some similar measure to prevent the always grave and occasionally fatal anaphylactic shock following absorption of the fluid from the cyst.

Although, owing to the development of the public water supply and slaughterhouse sanitation, infestation with Echinococcus has been rare in this country, there is ground for the belief that with development of the wood-growing industry now in progress in the United States and Canada hydatid disease will be on the increase in both countries.

Begg [24] discussed pyelography in cases of renal hydatid cysts.

When the echinococcus cyst is intact and communicates with a calix, the pyelographic appearances of the various types of cysts are as fol-

23. Tenenbaum, Joseph: Echinococcus Cyst of Kidney, J. A. M. A. **108**:1704-1705 (May 15) 1937.

24. Begg, R. C.: Pyelography in Renal Hydatids, Brit. J. Surg. **24**:691-702 (April) 1937.

lows: In first type the communicating calix appears somewhat drawn out and rigid. It terminates abruptly at the rim of the calcified ring, showing neither diminution in bore nor dilatation. In the second type the calix does not terminate abruptly but ends in a crescentic or cup-shaped shadow on which the circular calcified ring rests like an acorn in its cup. In the third type the flamelike areas of shadow pass out into the area bounded by the circular calcified ring, and a definite circumferential ribbon of shadow may appear reenforcing the latter. In the fourth type, in rare cases, the flamelike or circumferential shadows may pass out directly from the abrupt termination of the calix, the crescentic area being absent.

In cases of open hydatid cyst the pyelographic appearances are quite characteristic, especially if an adequate amount of fluid is injected and the injection continued to the point where the patient feels the discomfort of pressure. The crescentic bulge then becomes continuous, with a dense shadow which is well defined and circular, and represents the cyst cavity proper. In cases, however, in which numerous and closely packed daughter cysts are present, little fluid runs in except in irregular patches, more particularly around the rim.

In cases in which there is no communication between the cyst and the pelvis, the appearances are not so characteristic. The pyelogram is similar in many cases to that produced by a solitary cyst or even by a tumor. The kidney may be displaced, complete calices may be obliterated by pressure and the ureter may be pushed inward toward or even across the vetebral column. Sometimes a cyst may push itself into the angle between two of the major calices, separating them in such a way that they form a right angle with each other.

The characteristic pyelographic appearance of a cyst in the calix is the presence of well defined minor calices separated from the lumen of the major calix by a filling defect representing the parasite, with or without flamelike shadows connecting the two.

In practice, pyelography is chiefly of value in determining the side, site and nature of an open cyst that has already been diagnosed by identification of hydatid material in the urine, or in cases of closed or pseudo-closed cysts, in which the typical ring shadow seen in the roentgenogram may indicate a lesion of the spleen, liver or kidney or a pararenal cyst.

Aneurysm.—McKay [25] reported a case of true aneurysm of the renal artery, the diagnosis having been made at operation when the sac ruptured as the pedicle of the kidney was being isolated. The occurrence

25. McKay, R. W.: True Aneurysm of the Renal Artery, J. Urol. **37**:783-789 (June) 1937.

of renal aneurysm is extremely uncommon, and its preoperative diagnosis is difficult and is made only in a small percentage of cases. In about 50 per cent of the cases of aneurysm there has been a previous severe trauma to the lumbar region on the side affected. This condition is a great deal more common as an etiologic factor than syphilis or arteriosclerosis. Pain, hematuria and a dense, ringlike roentgenographic shadow with rarefaction in its center are suggestive of the diagnosis. If a larger aneurysm exists, a pulsating tumor and bruit make the diagnosis more certain. Treatment consists of nephrectomy when that is possible. Unfortunately, a small aneurysm is seldom diagnosed until hemorrhage at the operating table makes one suspicious or aware of its existence.

Trauma.—Stirling and Lands [26] carried out experimental studies on cats and dogs with a view to determining more precisely the types of secondary factors at work following various types of trauma of the kidney. They divided these injuries into four types: (1) mild injuries, chiefly perifascial, with only a slight effect on the fibrous capsule or the parenchyma; (2) rupture of the fibrous capsule, with small tears of the cortex; (3) serious ruptures, some of these involving the renal pelvis, and (4) pulpification of the renal parenchyma. The most striking point in the study was the discovery in the important third group that the resistance which the kidney offers to ruptures is, for the most part, due to protection which is given by the perirenal fascia and, more particularly, by its fibrous capsule. The force necessary to produce rupture of the kidney is essentially that which will shatter the capsule. All animals survived the experiments, and in each blood was found in the urine. When they were killed, cicatrization was already well advanced, and fat was found incorporated within the cicatrized renal tissue. The experiments effectively demonstrated the value of fat as a hemostatic agent in tearing of the kidney. Catgut ribbon ligatures were found to be of value in this kind of lesion, and no significant retraction of the organ followed their use. Attention must be drawn to the frequency with which renal degeneration follows extensive traumatism, manifesting itself by partial or incomplete necrosis of the renal cortex. This is probably due to the mode of distribution of the blood, since limited portions of the cortex decompose rapidly and produce a profound toxemia. These facts demonstrate the value of débridement and of drainage in all such lesions, for these measures tend to diminish the possibility of toxic absorption following injury to the renal cortex.

Study of the differential blood count during the days following experimental traumatism suggests that serious renal lesions are liable to be followed by a persistent anemia unrelated to hemorrhage. The

26. Stirling, W. C., and Lands, A. M.: Étude experimentale des facteurs secondaires aux traumatismes des reins, J. d'urol. **43**:304-312 (April) 1937.

number of erythrocytes per cubic centimeter of blood in the experimental animals fell rapidly during the first three or four days and remained low until about the thirteenth day, when it slowly rose again. In the control animals, in which the kidney was exposed but not traumatized, the number of erythrocytes was in no way modified. The number of leukocytes in both groups underwent considerable variations, usually in inverse ratio to the erythrocyte count but without any precise significance being discernible. It is impossible to state whether the anemia was due to toxic destruction of the kidney or to diminished hematopoiesis. Clinical findings of certain authors suggest the possibility that degenerative modifications of the kidney produce some toxic agent capable of exerting an unfavorable influence on the number of erythrocytes. The authors emphasized the importance of making frequent reexaminations of the blood after traumatism of the kidney has occurred.

With reference to treatment, injuries of types 1 and 2 can be handled expectantly; they seldom are seen by the surgeon, since hematuria is negligible. Those of type 3 as a rule require surgical intervention, but the tendency today is toward conservative intervention, which has become the rule since pyelography has made exact preoperative diagnosis possible. About two thirds of renal injuries are susceptible to conservative treatment. In cases of grave lesion with the urographic picture of rupture of the renal pelvis, with persistent hemorrhage and a state of shock, with lowered blood pressure and with a lowered erythrocyte count, conservative treatment with reparation of the ruptured tissue and drainage will in many cases secure restoration of function to the kidney. Transfusion of blood may be necessary, with recourse to the injection of serum, the application of artificial heat and the administration of sedatives. Plenty of time should be allowed for these measures before one resorts to nephrectomy. It should be thoroughly understood that surgical intervention in these cases does not necessarily imply nephrectomy but allows the surgeon to arrest hemorrhage and to repair, drain and conserve the kidney. In injuries of type 4, however, the only treatment possible is usually nephrectomy.

Ureteropyelic Dynamism.—Franche, Falcoiano and Chipail [27] made an exhaustive experimental study of ureteropyelic dynamism, as the result of which they reject as erroneous certain ideas that have recently been put forward by other authors on the subject. Notable among these ideas is the view that sympathectomy, whether by knife or by chemical means, can lead only to pure disturbances of dynamism in the ureter and pelvis, without producing any mechanical obstruction.

27. Franche, O.; Falcoiano, N., and Chipail, G.: Le problème expérimental due dynamisme urétéro-pyélique, J. d'urol. **43**:430-438 (May); 501-513 (June) 1937.

No conclusive proof of such a statement has ever been brought forward. Franche and his associates pointed out that when the result of sympathectomy is hydronephrosis caused by the appearance of stenosis (due to sclerosis of the ureteral wall or to a process of periureteritis), it is not justifiable to say that this stenosis is not of mechanical origin just because at the same time the dynamism of the ureter and pelvis is disturbed.

Their guiding principle in the study of this problem was the creation of numerous and varied causes of disturbance of ureteropyelic dynamism, intensive research of the obstacles produced in the ureter by these means and discovery of the dynamic disturbance by pyeloscopy as the best means of obtaining information in this field.

The experiments fall into four groups: (1) surgical sympathectomy, (2) permenent excitation of the ureter by means of a metallic or silken ring, (3) chemical sympathectomy and (4) crushing of the ureter by a hemostatic forceps. All observations were carefully controlled.

In all experiments detailed in the first two articles of this series, an anatomic modification was found above the point of sympathectomy, consisting of typical ureterohydronephrosis, always coinciding with an obstruction at the level of the sympathectomy. The caliber of this stricture was so uniformly that of a no. 12 sound that the authors were at first tempted to believe that the stenosis always leads to ureterohydronephrosis when just that caliber is reached. They later discovered, however, after a great number of experiments, that the stricture must fulfil certain conditions in order to produce ureteropyelic dilatation.

Among the 4 cases in which pyeloscopy was done, they found 1 in which an obstruction of the ureter could be observed, without an accompanying dynamic disturbance, while in the other 3 the disturbance of ureteral dynamism was absolutely typical.

The most important fact observed was that ureteropyelic dilatation, occurring quite early in most of the cases, may be produced in others only at a later period. While the earlier cases gave evidence of ureterohydronephrosis twenty days after sympathectomy, in the last of the series of 8 cases under consideration this condition was still absent forty-seven days after sympathectomy but became evident on the sixty-seventh day.

From the series of 8 experiments thus far detailed, the authors reached the following conclusions: 1. Whenever periureteral sympathectomy leads to ureterohydronephrosis, a mechanical obstruction is present. 2. In the majority of cases, after sympathectomy evident disturbance of dynamism is produced, consisting of spasms along the entire length of the ureter, of peristaltic and antiperistaltic movements

and of functional pyelic retention. These disturbances varied in the different examinations and sometimes even during the course of one and the same examination. 3. Sometimes these disturbances of dynamism may be altogether wanting after a sympathectomy correctly executed and followed by a characteristic ureteropyelic dilatation.

AMICROBIC RENAL PYURIA

Schaffhauser [28] discussed amicrobic renal pyuria based on studies of literature (19 personal cases observed at Professor Clairmont's clinic in Zurich and in Professor Wildbolz' clinic in Berne) and on experimental work. Views on amicrobic renal pyuria have changed in recent years. The occurrence of amicrobic urine in connection with renal tuberculosis is not uncommon. Separated urine, sterile on common culture mediums, was usually considered pathognomonic for tuberculosis, but such deductions are not necessarily true.

It has been ascertained by clinical, bacteriologic and histologic evidence that there exists a purulent disease of one or both sides of the upper part of the urinary tract, with accompanying serious cystitis, mostly without fever and of great chronicity, in which neither a direct smear nor an aerobic or anaerobic culture discloses microbes and in which a tuberculosis of the urinary tract can be excluded. Scandinavian authors (Söderlund, Galtin, Runeberg and Troell) were the first to report on nontuberculous amicrobic pyurias. Schaffhauser's 19 personal cases show such a conformity with Söderlund's cases that amicrobic pyuria can be accepted as a pathologic entity. The etiology of the disease is as yet not fully known. Schaffhauser expressed the belief that in some cases an atypical streptococcic infection may be the etiologic agent. In some instances streptococci could be cultured on Rosenow's broth. In 3 cases inoculation of purulent urinary sediment of patients having amicrobic pyuria into the renal pelvis of dogs caused chronic streptococcic pyelitis. It is important to know that unilateral amicrobic pyuria occurs, because in not a few instances kidneys have been erroneously removed when tuberculosis was thought to be present. The therapy of choice for amicrobic pyuria is the injection of small doses of arsphenamine. In every one of the patients so treated in a series reported by Wildbolz, recovery was rapid and definite.

To be distinguished from amicrobic pyuria are the amicrobic stages of acute or chronic infections of the kidney or renal pelvis, in which the original microbe can be found only after repeated cultures or sometimes not at all. The etiology of these cases is not uniform.

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28. Schaffhauser, F.: Die sogenannten abakteriellen renalen Pyurien, Ztschr. f. urol. Chir. u. Gynäk. **43**:83-140, 1937.

URETER

Anomalies.—Shih [29] stated that postcaval ureter is an extremely rare condition. Hochstetter in 1893 first reported a case in an infant a few weeks of age. Up to 1935 there had been a total of only 15 recorded cases, reported mainly in the anatomic and pathologic journals. In 11 instances the condition was discovered during anatomic dissections or at postmortem examinations.

Shih reported a case which is the fifth of its kind found at the time of operation. At operation the kidney was found to be badly diseased. The upper portion of the ureter was much dilated and lay close to the lateral border of the inferior vena cava. Instead of maintaining its lateral position, it passed posteriorly behind the vena cava and then forward between the vena cava and the abdominal aorta, above their points of bifurcation. Winding anteriorly, it again crossed the vein to resume its normal course to the urinary bladder. The portion of the ureter which wound around the vena cava was not dilated and was intimately adherent to the great vessels. In view of the definite evidence of disease of the kidney and the technical difficulties which would have occurred in freeing the ureter from the great vessels and in reuniting it in its usual position, it was considered best to remove the right kidney. Nephrectomy was carried out in the usual manner. The patient stood the operation well and made an uneventful recovery.

In addition to interest arising from its developmental aspects, this anomaly is of definite clinical significance. In the majority of cases, hydronephrosis and hydro-ureter of varying degrees have been present. If sufficient time were allowed to elapse, it is probable that the effect of back pressure resulting from compression of the ureter by the inferior vena cava would be evident in every instance. Damage to the kidney is further accentuated when obstruction is complicated by infection.

In order to save the kidney, early recognition of the anomaly and institution of operative correction is necessary. The procedure of choice, whenever possible, is to divide the ureter, disengage it from the vena cava and reestablish its continuity.

Stones.—Emmett [30] stated that manipulation of ureteral stones may be divided arbitrarily into two types, passive and active. Passive manipulation includes such procedures as the passage of ureteral catheters, the dilatation of the ureter below the stone with catheters or bulbs or the injection of lubricants of various kinds into the ureter below the

29. Shih, H. E.: Postcaval Ureter, J. Urol. **38**:61-66 (July) 1937.

30. Emmett, J. L.: Technical Points to Promote Safety in Manipulation of Ureteral Stone, Proc. Staff Meet., Mayo Clin. **12**:449-453 (July 21) 1937.

stone. By active manipulation is meant passage of instruments which actually grasp the stone and withdraw it; for instance, one may pass several ureteral catheters beyond the stone, twisting them so as to enmesh it and then withdraw it, or one may pass various types of ureteral stone extractors to engage the stone and withdraw it.

The passive type of manipulation is not difficult to perform and seldom presents technical difficulties to the surgeon, but it also is seldom efficient unless the stone is small and the patient is willing to endure repeated attacks of colic over varying periods of time before the stone is finally passed or removed by open operation. The active type of manipulation is successful in a high percentage of cases if done skilfully and with great care. However, if painstaking technic and the utmost gentleness are not exercised, serious difficulties and complications may ensue.

With regard to the size of the stone, Thompson emphasized repeatedly a rule to follow; he stated that the deciding factor is not the size of the stone but rather the diameter of the ureter, and he insisted that no stone should be manipulated if there is not sufficient room in the ureter. One method of deciding this point is by the preliminary passage of ureteral catheters alongside the stone. It should be possible to pass two no. 5 ureteral catheters easily beyond the stone before passage of the stone extractor is attempted. When the extractor is passed, it should be passed gently and should never be forced. If these factors are kept in mind, a minimum of difficulty will be encountered.

Even though these rules are adhered to, however, a third difficulty may be encountered. This is the possibility that the stone may become arrested somewhere in the ureter in the course of its withdrawal. This is a rather uncommon occurrence, but it does happen often enough to be important. One must be careful not to exert too much traction in such a case or injury to the ureter may occur. Such a situation presents a real problem to the surgeon and may necessitate ureterolithotomy. Occasionally stones enmeshed in the stone extractor became arrested at the ureterovesical junction and were removed successfully by means of a two stage procedure without undue trauma or resort to open operation.

In 1 case two no. 5 ureteral catheters passed easily beyond the stone. The Councill stone extractor was introduced into the ureteral meatus, and the wires were expanded to dilate the intramural portion of the ureter. Then the extractor was passed easily beyond the stone, which was engaged readily. As it was being withdrawn, it became arrested at the proximal end of the intramural portion of the ureter and could not be removed. A roentgenogram made at this time revealed the stone enmeshed in the basket of the extractor in this position. In spite of

dilatation with the basket of the extractor, which was lying in the intramural portion of the ureter, the stone could not be dislodged. It was thought that if the extractor was left in place for twenty-four hours, sufficient dilatation would result to extract the stone. Accordingly this was done. The handle of the extractor was removed, and the cystoscope was withdrawn. A small no. 16 ureteral catheter was passed to the bladder alongside the extractor and tied in place. The patient had practically no discomfort during the night, no renal colic, no elevation of pulse and little elevation of temperature. He was returned to the cystoscopic room the following morning, and the cystoscope was introduced by threading the stem of the extractor through its lumen. With moderate traction the stone was withdrawn successfully, and two no. 5 ureteral catheters were immediately passed up the ureter and left in place for forty-eight hours. Convalescence was uneventful, and after the catheters were removed the patient had no further pain. Suitable urinary antiseptics were given postoperatively to eradicate urinary infection.

Jarman and Scott [31] discussed avertin (tribromethanol) as a relaxing agent in manipulative removal of ureteral calculi. After admission to the hospital the patient is routinely given disodium hydrogen phosphate and methenamine, even though infection is absent. Fluids are forced, and medication is given, if necessary, to relieve the pain. A wax tip bougie is passed to confirm the diagnosis, and at the same time the distance of the obstruction above the uretero-vesical orifice is measured. One no. 5 French ureteral catheter is then passed by the obstruction to the kidney, when possible. This insures good drainage and protects the kidney. After this, bougies or catheters of such size and number as the obstructed ureter will permit are passed to the kidney, the most frequent combination of instruments being one no. 5 French ureteral catheter and two ureteral bougies or catheters of the same size or a little larger.

The patient is then given the injection of avertin. This solution is prepared, freshly and aseptically, by dissolving 1 Gm. of avertin crystals in 50 cc. of warm, sterile, distilled water. This 2 per cent solution is injected, while warm, directly through the indwelling catheter into the renal pelvis. The amount injected is determined by the pain produced from moderate distention of the pelvis. The catheter is then plugged, and the patient is requested to sit upright in order to facilitate the passage of some of the solution down along the ureter. This is

31. Jarman, W. D., and Scott, W. W.: The Introduction of Avertin as a Relaxing Agent in the Manipulative Removal of Ureteral Calculi, J. Urol. **83**:111-117 (July) 1937.

allowed to remain in contact with the pelvis and ureter approximately fifteen minutes. After this the instruments are withdrawn, at which time they are slowly twisted and more solution is injected directly into the lumen of the ureter, thus insuring a more adequate perfusion of the ureter with the solution. The patient is instructed to void in the erect posture.

Of 27 consecutive cases in which multiple catheters and instillations of this solution were used, the calculus was recovered in 25 (92.5 per cent). In 13 cases (48.1 per cent) the stone was recovered as soon as the patient voided.

PROSTATE

Hypertrophy.—Thompson [32] reported 2 cases in which unusual intravesical projection of the enlarged prostate gland was evident. Until recent years such enlargements were of little interest to urologists, for they were easily enucleated during the course of suprapubic prostatectomy. In contrast, such projections are now sometimes difficult to remove by transurethral resection and often one is overlooked and results in persistent symptoms and unsatisfactory vesical function. Bizarre filling defects are sometimes noted in the cystogram, and at times granulation tissue is superimposed on the enlargement and is mistaken for vesical neoplasm. Thorough removal of all intravesical prostatic tissue during the course of transurethral resection is essential to a good result.

Clarke [33] stated that interest in the old theory that prostatic hypertrophy is caused by some abnormality of the endocrine system is being revived by the recent isolation of androgen and by the experimental work on prostatic enlargement which this discovery permits. Much of this work is unconfirmed, and some of it is contradictory. According to the theory advanced at the Cleveland Clinic, prostatic hypertrophy is caused by diminution in testicular output of a substance which is designated by McCullagh and his associates [34] as inhibin. This water-soluble substance restrains the output of gonadotropic principle from the pituitary gland, which in turn stimulates the formation of fat-soluble androgen in the testes. Excess of the latter is supposed to be responsible for prostatic stimulation and hypertrophy. Therefore a commercial preparation known as "contruin," said to contain this water-soluble

32. Thompson, G. J.: Unusual Intravesical Projection of the Enlarged Prostate Gland, J. Urol. **37**:367-371 (March) 1937.

33. Clarke, Ruscoe: The Prostate and the Endocrines a Control Series, Brit. J. Urol. **9**:254-271 (Sept.) 1937.

34. McCullagh, R. D.: Dual Endocrine Activity of Testes, Science **76**:19 (July 1) 1932. Lower, W. E.; McCullagh, D. R., and Walsh, E. L.: Further Report on the Hormonic Control of Prostatic Function, Tr. Am. A. Genito-Urin. Surgeons **27**:15, 1934.

testicular substance, is being used to break down the gonadotropic activity of the pituitary gland, causing a reduction in androgen and thus preventing further prostatic enlargement.

In other clinics androgen (fat-soluble androsterone) is being used on the experimental evidence that it counteracts the effect of estrogen, which produces enlargement. If the theory advanced by the Cleveland Clinic is correct, use of this fat-soluble androgen should increase rather than decrease the hypertrophy. Therefore, the argument that use of endocrine substances will do no harm is unsound if they are effective. Unwarranted claims as to their effectiveness may be made in the absence of control series of untreated patients having prostatic disease when it is realized that the course of prostatic enlargement, both histologically and symptomatically, is extremely variable.

To offer as a control the progress of untreated prostatism, Clarke made a careful study of 93 patients who were followed over a period averaging 4.3 years. The majority had early enlargement uncomplicated by gross infection or failure of bladder function—a condition which might be considered ideal for endocrine therapy. The cases were divided into four groups.

Group 1 consisted of 31 cases in which the diagnosis was in doubt when the patient was first seen. This group included a number of cases in which the symptoms were at first incidental to some other condition. In all, however, convincing signs or symptoms of prostatic obstruction developed during the period of observation.

Group 2 consisted of 36 cases in which when the patient was first seen the diagnosis was definite, but the amount of residual urine was small, infection was slight or absent and no other complications were present.

Group 3 consisted of 15 cases in which the diagnosis was definite; over 100 cc. of residual urine was present, or there was marked infection or some other complication.

Group 4 consisted of 11 cases in which the patients were first seen during or immediately after acute chronic total urinary retention.

In the first two groups surgical intervention was not immediately indicated by ordinary standards. Groups 3 and 4 consisted of cases in which surgical intervention would ordinarily be advised. In most of these cases the patients had refused operation, or operation had been delayed for some other reason. Diagnosis was established on the basis of symptomatology, rectal examination and cystoscopic examination. The average age of the patients was 63.2 years; the average duration of symptoms before observation, 2.56 years, and the average period of observation, 4.3 years. No treatment of any sort was prescribed.

The term "cure" cannot be used in describing the progress of these patients. Therefore the term "improvement" is substituted, and this is based on the progress of the symptoms. In no case was there any evidence of actual shrinkage of the gland. Of the 67 patients in groups 1 and 2, the condition in 47 improved and in 10 it was stationary for an average duration of 3.58 years. Of the 26 patients in groups 3 and 4, the condition in 15 improved and in 8 it was stationary for an average duration of 2.64 years. A more detailed classification based on both symptoms and objective signs of the disease is shown in the accompanying table.

These figures show how easily one might be misled in interpreting the results of endocrine therapy. A large number of patients who have prostatic disease can be relieved for a variable period by general hygiene, massage, heat or instrumentation. A large number in this series showed a sustained improvement after instrumentation alone (cystoscopy).

Detailed Classification of the Course of the Disease (from Clarke)

Course	Groups I and II	Groups III and IV	Total
(*a*) Rapid sustained improvement	14	2	16
(*b*) General improvement	7	2	9
(*c*) Improved, with remission	15	8	23
(*d*) Improved, later progressive	12	6	18
(*e*) Slowly progressive	11	1	12
(*f*) Gradually progressive	6	6	12
(*g*) Rapidly progressive	2	1	3

Therefore, control series are desirable before any evaluation of the efficiency of endocrine therapy is made, and patients so treated should be studied for a considerable period, not less than five years.

Middleton [35] reported the removal of a prostate weighing 557 Gm. from a patient aged 72. This enormous prostate was almost a pound heavier than the greatest mass of tissue ever removed transurethrally up to now, even with multiple operations. Middleton advised deliberate fragmentation of huge prostates as the easiest, safest method of operation.

This is the largest prostate ever removed surgically. The only larger gland described in medical literature was that reported by Douglas, which weighed 673 Gm. In his case, however, the patient failed to survive suprapubic cystotomy, and the prostate was obtained and studied at necropsy. Freyer, of England, in 1908 removed a prostate weighing 529 Gm., which was the largest surgical specimen previous to the present case.

35. Middleton, R. P.: How Large Is the Hyperplastic Prostate? Report of the Largest Hypertrophied Prostate Ever Surgically Removed, J. A. M. A. **108**: 1967-1968 (June 5) 1937.

In the early years of Irwin's [36] urological work, he performed the two stage operation in about 10 per cent of his cases, using the Thomson-Walker open operation or the one stage blind method in about 90 per cent. Finding the results more satisfactory in the two stage operation, which he originally used only in the patients who were so-called bad risks, he gradually used this method more and more, until at the present time he employs it in the majority of prostatectomies. Many complications which follow prostatectomy, some of which may be fatal, are avoidable by using the two stage operation.

Irwin reported a series of 158 cases in which prostatectomy was performed. In the case of patients who did not have much residual urine, cystotomy was done two days after their admission to the hospital. When there was obstruction enough to cause a large quantity of residual urine, the bladder was gradually emptied and afterward drained by an indwelling catheter for two or more days before the first operation was performed.

Once cystotomy had been done there was no urgency about prostatectomy, and the length of the interval between the two was determined by the patient's condition after the first operation, the general clinical findings, the state of the suprapubic wound and the results of the tests of renal efficiency. The interval between the two operations was seven days in 110 cases (69 per cent) in the series and fourteen days in 32 (20 per cent), while in the remaining cases, with few exceptions, the interval varied from eight to twenty-one days.

Carcinoma.—Ferguson [37] discussed diagnosis and treatment of cancer of the prostate when the tumor is less than 4 cm. in diameter and the patient presents no subective or objective signs of metastasis. For this purpose Ferguson has attempted to evaluate aspiration biopsy as a method of early pathologic diagnosis and to report the results obtained in the treatment of cancer of the prostate by precise instrumental implantation of gold seeds of radon through the open bladder.

The only function of aspiration biopsy is to differentiate neoplastic and non-neoplastic tissue. Many regard the procedure as a failure because they expect more information than this. For the purpose of evaluating this procedure, a comparison was made of the results in three series of consecutive cases of prostatic involvement in which aspiration biopsy was performed under different circumstances. In the first series, consisting of 50 cases, the specimens were obtained at the

36. Irwin, W. K.: Prostatectomy by the Two-Stage Method: A Survey of One Hundred and Fifty-Eight Cases, Brit. M. J. **1**:261-262 (Feb. 6) 1937.

37. Ferguson, R. S.: Diagnosis and Treatment of Early Carcinoma of the Prostate, J. Urol. **37**:774-782 (June) 1937.

Memorial Hospital by a single surgeon and were interpreted by a pathologist of long experience in the diagnosis of cancer, who had already examined more than 5,000 specimens obtained by aspiration from tumors in other parts of the body. In the second series, consisting of 50 cases, the specimens were also obtained at the Memorial Hospital by the same surgeon and were interpreted by the same pathologist, the study being begun about six months after the completion of the first investigation. The results reflect the value of experience with this method. In the third series, consisting of 36 recent cases from the service of Dr. Keyes at the New York Hospital, the specimens were obtained by 7 different resident and attending surgeons who were attempting to learn the technic by routine biopsy of all persons admitted with prostatism.

Diagnosable tissue was obtained in 39, or 78 per cent, of the cases in the first series, and no tissue was found in 11. Of the 39 cases in which tissue was obtained, a positive diagnosis of cancer of the prostate was made in 28. No cancer was found in 11. Twenty-seven of the 28 patients with a diagnosis of cancer of the prostate died, and at the time the report was made 1 patient was alive and without evidence of active disease. In the 11 cases in which tissue was obtained by biopsy and in which no cancer was found, no patient was subsequently proved to have cancer of the prostate.

Diagnosable tissue was obtained in 43, or 86 per cent, of the cases in the second series, and no tissue was found in 7. Of the 43 cases in which diagnosable tissue was obtained, a positive diagnosis of cancer was made in 31. Thirty of the 31 patients with a diagnosis of cancer subsequently died of disease, and 1 was alive at the end of thirty-four months but had demonstrable metastasis. In none of the 12 cases in which diagnosable tissue was obtained but no cancer found was cancer of the prostate subsequently proved.

In the third series of cases, in which aspiration biopsy was carried out by surgeons and pathologists of no previous experience with the method, diagnosable tissue was found in 27, or 77 per cent, of the cases, and no tissue was found in 9. Of the 27 cases in which tissue was obtained, a positive diagnosis of cancer was made in 10. Nine of the patients were subsequently proved to have the disease, while 1, on the basis of clinical behavior, was considered not to have cancer.

Treatment of early cancer of the prostate by cystotomy and retrograde instrumental implantation of gold seeds of radon was devised after a study of the biologic effect of different applicators of radium on the tissues in 50 cases of cancer of the prostate in which autopsy was later performed. With this method of treatment, the bladder is opened under spinal anesthesia, and the trigon and neck of the bladder

are inspected. The seeding instrument is then introduced, the sound entering the urethra retrogradely, dilating it slightly. The plate is held firmly against the neck of the bladder by an assistant. The tumor will then be felt surrounding the sound and under the plate. Needles are then introduced through the cylinders of the plate which overlie the tumor. Their placement is determined by palpation, as they are pushed through the tumor. When all have been used, the instrument is withdrawn, and the bladder is closed with suprapubic drainage. The tissue dose delivered by this technic will be found to equal or slightly exceed the required dose for the tumor, considered as a sphere of a given diameter. The total average dose of radon is about 25 millicuries and varies from 15 to 40 millicuries.

The first of these operations was done by Dr. Keyes on May 6, 1931. Since that time the records of 43 patients with cancer of the prostate who were operated on by this method have been collected. Of the 43 patients, 14 were operated on more than three years ago. At the time the author's report was made, 4 were alive and well. Of the 14 patients operated on more than three years ago, 4 were alive and without evidence of active cancer of the prostate more than thirty-six months. The remaining 10 patients subsequently died of cancer of the prostate, most of them with metastasis.

The status of the 29 patients operated on less than three years ago was reported as follows: patients alive and without evidence of recurrence or metastasis for less than one year, 2; for from one to two years, 8, and from two to three years, 4; patients alive with local recurrence or metastasis for from one to two years, 2, and from two to three years, 3. The deaths in this group occurred as follows: 1 postoperative death, 5 deaths in less than one year, 2 in from one to two years and 2 in from two to three years.

These results have not been achieved without accident. There was 1 postoperative death.

Prostatic Resection.—Plaggemeyer and Weltman [38] discussed the limitations of resection of the prostate gland. Their paper is not a statistical one but is intended as a general survey of the subject to date. Their personal views are based on a series of 600 transurethral resections, the data in each case having been carefully analyzed and evaluated in relationship to the observations of their colleagues throughout the country.

Plaggemeyer and Weltman prefer suprapubic enucleation in cases in which the gland is grossly enlarged and in which, for any reason,

38. Plaggemeyer, H. W., and Weltman, C. G.: The Limitations of Transurethral Resection of the Prostate Gland, J. Urol. **38**:389-396 (Oct.) 1937.

the bladder had to be opened, such as in cases of stone in the bladder, diverticulum, marked gross infection, etc. There is no indication for transurethral removal after the bladder has been once opened, except in cases of carcinoma, fibrous bars, small fibrous prostates and such obstructions in which suprapubic enucleation would be difficult. In these cases resection should be done anyway. The greatest trouble continues to be sepsis, as it was two years ago at the time of a previous report.

The authors stated that the caliber of an unstretched urethra is equal to that of a no. 25 French catheter and the caliber of a slightly stretched urethra is equal to that of a no. 26 French catheter. Up to the present, most resectionists have been using a no. 28 French catheter for a fairly long period, jamming the mucous membrane and crowding out the local blood supply by pressure, thus heating the membrane, which, having temporarily lost its blood supply by pressure, has also lost its resistance and has a tendency to become "cooked" or "toasted." To prevent this, Plaggemeyer and Weltman use the no. 28 French catheter rapidly and for a minimum amount of time, working fast and getting out a maximum of tissue; they then shift to the no. 24 French catheter and trim the edges, if necessary, and make a final inspection for bleeders. This procedure tends to insure the maximum of success with a minimum of surgical trauma. They resect the vas deferens as a routine procedure and report that they have never had epididymitis develop following this procedure, although occasionally funiculitis occurs, which readily subsides. The large bilateral lobe, extravesical type of adenoma, with no middle lobe, is the most difficult to resect. This type must be excavated (shelled out), keeping distal to the neck of the bladder lest it be cut away and result in extravasation of urine. At least three quarters of the gland must be removed to secure results. The enormous middle lobe causes trouble at times, until enough is cut away to see the landmarks clearly.

Plaggemeyer and Weltman offer the following factors as probable contraindications to resection: (1) large extravesical prostates; (2) large intravesical prostates extending backward under the trigon in an embarrassing proximity to the ureteral orifice; (3) deeply embedded prostatic calculi; (4) large vesical calculi, with foully infected bladder; (5) dependent diverticula of the bladder, and (6) patients in their early fifties, with a mild diffuse infection and possible beginning adenoma. The infection should be treated first; otherwise, having carried out a resection, the operator may find himself with an unpleasant responsibility for eradicating the infection, a matter of two years of work.

Hugh Cabot put the whole matter fairly and succinctly when he stated:

> If the operation is to be done by the general surgeon or the occasional operator on the prostate, then the safest way is with the knife, with a 15 per cent mortality. If it is to be done by experts, then there are now on record well over 8,000 cases in total, done with a mortality of less than 2 per cent, including all risks, and a hospital confinement of a week or even less in some rare cases, with functional results as good, or even better, than that obtained by older methods.

Thompson [39] emphasized the necessity for care in the passage of instruments through the anterior portion of the urethra. It may be unwise or difficult to perform transurethral prostatic resection when there is an irreducible intrascrotal hernia, when the urethra is unusually small (either normally or from disease) or is unusually long, as in an obese man with a thick perineum, or when there is complete or relative fixation of the hips secondary to arthritic changes. Cabot suggested that perineal urethrotomy through a small longitudinal incision into the bulbous portion of the urethra might be employed in cases of this type.

Thompson reported the case of a man aged 62 who had a large carcinoma of the prostate which caused obstruction. Transurethral prostatic resection was performed in February 1934, at which time 11 Gm. of tissue was removed. Microscopic examination revealed adenocarcinoma, graded 3 on a basis of grades 1 to 4. Convalescence was uneventful, and the patient did well until a short time before his return in May 1937, at which time more than three years had elapsed since the original transurethral operation. There was still no evidence of metastasis. Because of the difficulty in passing an instrument through the anterior portion of the urethra and into the bladder, the urethra was opened through a small incision in the central point of the perineum. A resectoscope of large caliber was inserted through this incision and was passed into the bladder. Twenty-three grams of tissue was removed with ease. At the conclusion of this procedure a catheter was passed through the anterior part of the urethra into the bladder, and the edges of the small incision in the perineum falling into direct apposition did not require suture. On the fourth day the urethral catheter was removed, and the patient voided a large stream. There was no leakage at any time from the perineum. The patient was dismissed from the hospital on the fifth postoperative day, at which time he voided freely and had no residual urine. Cabot [40] mentioned that

39. Thompson, G. J.: Perineal Prostatic Resection, Proc. Staff Meet., Mayo Clin. **12**:360-362 (June 9) 1937.

40. Cabot, Hugh, in discussion on Thompson,[39] pp. 362-363.

the procedure used in this case was similar to that advocated by Bigelow a number of years ago for the performance of litholapaxy. It seems likely that this procedure would greatly facilitate the performance of prostatic resection when, for any reason, it is not feasible or it is difficult to pass instruments of large caliber through the anterior portion of the urethra.

Boyd [41] reported 2 cases of urethral injury from the use of the metal covered bakelite sheath in transurethral prostatic resection. One patient complained of a most unusual, frequently recurring burning in his rectum after operation which continued intermittently for four weeks; the urine remained cloudy, especially the first glass; there was a little loss of control of the urine when the irritation of the neck of the bladder was most annoying. At the end of the fourth week examination with the panendoscope revealed rather extensive but seemingly superficial injury of the floor and of the lower part of the lateral walls of the membranous portion of the urethra. In another patient (spinal anesthesia) the right leg jerked into extension twice during the operation, and three weeks after operation the panendoscope showed definite injury of the lower right side of the membranous portion of the urethra, mucus being adherent along the lower right side of the whole length of this portion.

During these two operations each of the telescopes used was so badly damaged by the current jumping from the loop to a point near the lens that it had to be repaired before it could be used again. Both of them were found to have a hole through the metal.

Walker [42] stated that there are two chief danger points in carrying out prostatic resection: the region of the trigon and the posterior portion of the urethra. An injudicious cut in the trigon will open up the space of Denonvillier, and a cut in the posterior portion of the urethra will perforate the rectum. Of these two disasters, the former should be feared more. Two of Walker's patients have passed urine by rectum a few days after resection without being any the worse for their temporary fistula. Over 20 suffered from severe sepsis following resection, and, although he has no definite proof for this, Walker expressed the belief that in some of these cases of protracted sepsis the space of Denonvillier had been infected. In order to prevent this, when tissue is removed at the level of the sphincter the instrument should be kept horizontal and not dipped down into the bladder.

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41. Boyd, M. L.: Urethral Injury from Using the Metal Covered Bakelite Sheath in Transurethral Prostatic Resection, J. Urol. **38**:100-101 (July) 1937.

42. Walker, K. M.: Transurethral Resection of the Prostate: A Review of Fourteen Years' Work, Brit. M. J. **1**:901-903 (May 1) 1937.

Where a severe infection has existed prior to operation, if the urethra tolerates an indwelling catheter badly or if the patient is likely to resent catheterization, Walker combines resection with temporary suprapubic drainage. Not only does this allow adoption of far more efficient methods of treatment of sepsis but it relieves one of all fear of clot retention following the operation. Moreover, these gains are purchased at a small cost, for once the obstruction has been removed the suprapubic fistula will close in the course of a few days.

Walker employs resection in about 20 per cent of all cases of prostatic involvement, reserving it in particular for minor enlargements or for patients in whom, for one reason or another, it would be dangerous to perform prostatectomy. Because resection can be carried out in cases in which enucleation would be dangerous, it appears to him to be the most valuable of recent additions to the methods of treatment. When combined with temporary suprapubic cystotomy, local anesthesia being used, it is by far the safest of all the surgical attacks on the obstructing prostate and can be carried out on patients who formerly would have been condemned to catheterization for life or to permanent suprapubic drainage.

Pilcher and Sheard [43] developed a technic for determining the amount of blood lost at the time of operation by using the Cenco-Sheard-Sanford photelometer as well as by using direct spectrophotometric readings. In general, all bloody fluids and sponges, towels, etc., which contain blood are saved and the latter thoroughly washed with water in order to remove all the hemoglobin from them. The resultant liquid is then used for comparison with known standards, and the hemoglobin content is thereby determined. It was found that the maximal error with this method was approximately 5 per cent and was generally less than 3 per cent. In 1935 Pilcher studied a series of 55 cases in which transurethral prostatic resection was performed and found that approximately 479 cc. of blood was lost in each case. The average amount of tissue removed was 12.27 Gm., and the blood lost per gram of tissue removed was 39.03 cc. Subsequently Pilcher studied another series of 55 cases in which prostatic resection was performed with the use of the new instrument which Thompson designed. The average amount of blood lost in each of these cases was 291 cc. The average amount of tissue removed was 14.5 Gm., and the blood lost per gram of tissue removed was 20 cc. Pilcher then studied certain common abdominal operations and compared the amount of blood lost during these pro-

43. Pilcher, Frederick, Jr., and Sheard, Charles: Measurements on the Loss of Blood During Transurethral Prostatic Resection and Other Surgical Procedures, Determined by Spectrophotometric and Photelometric Methods, Proc. Staff Meet., Mayo Clin. **12**:209-213 (April 7) 1937.

cedures with the amount lost during prostatic resection. He found that the amount of blood lost during prostatic resection compared favorably with that lost during other surgical procedures of equal magnitude. The method for determining the amount of blood lost at the time of operation seems accurate and should be of value in determining the amount of blood lost under any similar circumstances. It appears that the amount of blood lost during prostatic resection is less than the amount lost when suprapubic prostatectomy is performed.

(To Be Continued)

CORRECTION

In the article by Drs. Gray and Heifetz entitled "Lymphoid Hyperplasia of the Appendix, with a Note on Its Role in Acute Appendicitis," in the November issue (ARCH. SURG. **35**:887, 1937), "fourteen thousand appendixes" in the second line of the first paragraph on page 900 should read "fourteen hundred."